RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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RADIOLOGY

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Vol. 51 AUGUST 1948 No. 2

Roentgen Therapy of Carcinoma of Female Urethra and Vulva[1]

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Seattle, Wash.

FROM A REVIEW OF the literature, it seems that external roentgen therapy has not been used in a systematic way for the treatment of the *primary lesion* of either carcinoma of the vulva or urethra. Some radiologists have indeed expressed amazement that it can be used without deleterious by-effects. In a paper on carcinoma of the vulva by Smith and Pollack from the Gynecological Service of Memorial Hospital, we find as late as January 1947 this sweeping statement: "The inadequacy of x-ray and radium in treating either the primary or metastatic foci of this condition is well known." A similar impression is gained from Berven's thorough discussion of the large group of vulvar carcinoma treated at the Radiumhemmet.

The reason for this misconception is probably an insufficient appreciation of the importance of the quality of the radiations used. Some of these lesions, because of their superficial location, may tempt the therapist to employ low-voltage irradiation. This will not be tolerated by the vulvar mucosa in doses necessary for sterilization, even if the entire tumor can be homogeneously irradiated. The material to be presented here will demonstrate that with radiation in the 200-kv. range a tumor-sterilizing dose can be delivered which is still tolerated by the sensitive vulvar mucosa. In spite of the small number of cases, we feel justified in discussing our experience. Our observations have been sufficiently uniform to lead us to certain conclusions in regard to the necessary tumor dose as well as to the limit of tissue tolerance.

There is no single procedure—surgery or irradiation—that can be considered as the method of choice in the treatment of the primary focus in carcinoma of the vulva and female urethra. The choice in the individual case depends on the location and extension of the lesion and the anticipated functional result following therapy. While the tumors are sufficiently radioresponsive to be controlled by radiotherapy, the morbidity following irradiation of the vulnerable vulvar mucosa must be taken into consideration. Adequate doses over the vulva cause rather severe and slowly subsiding reactions and may lead to mucosal atrophy with lowered resistance to local infection and irritation. Comparatively small carcinomas originating in the labia, clitoris, or posterior commissure are therefore better treated by radical excision. In this type of lesion radiation therapy is rather reserved for the more advanced stages, in which surgery cannot be expected to remove the entire lesion because of diffuse extension into the neighboring sub-

[1] From the Tumor Institute of the Swedish Hospital, Seattle, Wash. Presented at the Thirty-third Annual Meeting of the Radiological Society of North America, Boston, Mass., Nov. 30–Dec. 5, 1947.

TABLE I: ADVANCED CARCINOMA OF THE VULVA. ROENTGEN THERAPY: 200 KV., 2 MM. CU + 1 MM. AL; 60 CM. T.S.D.

Case; Year Treated; Age	Location	Histology	Total Dose to Vulva, (r/skin)	Field Size, cm.	Treatment, days	Primary Reaction	Late Result	Late Mucosal Condition	Remarks
1. 1940. 65 yr.	Large carcinoma of left major labium. Left inguinal node, 8 cm., fixed. Incomplete surgical removal	Epidermoid II	4,100 r	5 × 7	21	Moist epidermite, 30th–45th day	Well 7 years	Moderate atrophy and scarring. No subjective discomfort	4,500 r to left groin in 13 days
2. 1941. 65 yr.	Clitoris, postoperative. Bilateral extensive inguinal nodes	Epidermoid II	3,100 r	6 × 8	20	Membranous reaction, 27th–48th day	Died 1 yr. 2 mo. Extensive deep inguinal metastases	.....	4,450 r to right groin; 4,000 r to left groin
3. 1942. 57 yr.	Right major labium. Deep infiltration. Incomplete surgical removal	Epidermoid II	4,200 r	5 × 6	20	Membranous reaction, 20th–42nd day; urethral reaction, 30th–42nd day	Well 5 years	Excellent	Urethra in field
4. 1944. 49 yr.	Major labium, right. Incomplete surgical removal	Epidermoid II	4,400 r	5.5 diam.	25	Membranous reaction, 25th–44th day; no urethral reaction	Well 3 years	Good	Elephantiasis following inguinal dissection. Inguinal nodes positive
5. 1944. 46 yr.	Kraurosis, *leukoplakia*. Extensive carcinoma of clitoris with large inguinal nodes	Epidermoid II	4,500 r	4.5 diam.	18	Membranous reaction, 22nd–42nd (?) day	Died 1 yr. 3 mo. Extensive deep inguinal metastases	.....	Bilateral inguinal dissection
6. 1945. 39 yr.	Right major labium and posterior commissure. Severe leukorrhea	Epidermoid II	4,550 r	5 diam.	26	Mucosal reaction, 26th–86th (?) day	Well 1 yr. 2 mo.	Excellent	Bilateral inguinal dissection. Transitory edema of labia
7. 1946. 82 yr.	*Leukoplakia* and carcinoma of right major labium	Epidermoid	4,000 r	4.5 diam.	18	Membranous reaction, 16th–42nd day	Well 1 yr. 2 mo.	Excellent	.....
8. 1946. 57 yr.	Large carcinoma of entire vulva. Large bilateral nodes	Epidermoid III	4,800 r	6 diam.	26	21st–40th (?) day	Alive 9 months, with large abdominal mass	.....	4,725 r to right groin; 4,725 r to left groin

cutaneous structures. The curability by radiation therapy, even of advanced lesions in these locations, is reasonably good because of the comparatively low degree of differentiation of the epidermoid carcinomas usually encountered here. By careful adjustment of the treatment, the by-effect can be minimized to a degree that the tissue damage does not cause any appreciable permanent disability. Radiation therapy is also the procedure of choice in the treatment of lesions—even smaller ones—in the periurethral portion of the vulva, the surgical removal of which would necessitate the destruction of the urethra, with unsatisfactory functional results in many instances.

Carcinomas originating in the urethra itself represent a different histologic and clinical entity than periurethral carcinomas of the vulva. They more frequently originate from glandular structures, with secondary metaplasia into adenoacanthoma probably exhibiting a somewhat less marked response to irradiation. However, they cause symptoms of obstruction, pain, bleeding, and foreign-body sensation, comparatively early, at a stage when the actual tumor volume is still reasonably small and therefore can be included in a small field of irradiation. For this reason the reaction can be kept within reasonable limits of intensity and late tissue changes are minimized.

In accordance with these concepts, the cases which we selected for radiation therapy comprise early carcinomas of the urethra and advanced carcinomas of the vulva.

Our main interest in this discussion is centered on the urethral carcinomas, since the functional results obtained with local medium-voltage roentgen therapy in the opinion of some of our urological colleagues appear to be superior to those obtained with any other form of treatment—surgical or radiological—so far used. The cases of extensive vulvar carcinoma treated are included mainly because they have broadened our experience in regard to the tolerance of the vulvar mucosa when larger fields are used.

The management of the lymph nodes is a problem in itself, independent of the treatment of the primary lesion. It is omitted from the present discussion because our material is too small for any pertinent conclusions.

CARCINOMA OF THE VULVA

The details of 8 cases of advanced carcinoma of the vulva are summarized in Table I. Five of the patients are well to date for seven (Figs. 1–3), five, three, two and a half, and one and a quarter years, respectively; 1 (Case 8) is alive after nine months with extensive iliac metastases, the primary focus apparently primarily controlled; 2 died of extensive inguinal metastases.

The doses in the controlled cases varied between 4,000 and 4,500 r/skin given in twenty to twenty-six days to fields measuring 20 to 35 sq. cm. Mucosal reaction developed between sixteen and twenty-five days following the beginning of treatment; the moist skin reaction, when skin was included in the field (Case 1), around the thirtieth day. The reaction lasted longer than reactions in the upper respiratory mucosa and healing was not completed until the forty-second to the forty-fifth day. In one case only (Case 6) was the reaction severe enough to cause serious morbidity necessitating hospitalization. This case was complicated by a severe and uncontrollable leukorrhea, and the condition of the infected and macerated mucosa prior to treatment forewarned of difficulty. Radiation therapy was decided upon only because the lesion extended posteriorly so close to the anal ring that surgery would have involved a rectal resection with permanent colostomy. In this case the additional bilateral inguinal dissection, with temporary edema of the vulva, further aggravated the situation and caused a prolonged morbidity. In none of these other cases was the reaction out of proportion, in duration or intensity, to the accomplished result. The permanent mucosal changes are minimal. In none of these patients is there any remaining disability. The tissue

TABLE II: CARCINOMA OF FEMALE URETHRA AND URETHRAL CARUNCLE. ROENTGEN THERAPY: 200 KV., 2 MM. CU + 1 MM. AL; 60 CM. T.S.D.

Case; Year Treated; Age	Histology	Total Dose, r/skin	Treatment, days	Field Size, cm.	Primary Reaction	Result	Late Mucosal Condition
1. 1942. 61 yr.	Epidermoid III	5,650 r	20	3.5–4 diam.	Very massive primary reaction, 20th–64th day. Late necrosis 1 year later	Well 5 years	Slight stricture. Moderate atrophy and telangiectasia. Function good
2. 1943. 57 yr.	Adenoacanthoma	5,200 r	22	3.5 diam.	Mild, 28th–51st day. Late necrosis 6 months	Well 4 years	Function good. Very slight atrophy
3. 1945. 68 yr.	Adenoacanthoma	4,600 r	32	3 diam.	Mild, 37th–46th day	Well 2 years	Overflow incontinence. Mucosa excellent
4. 1947. 65 yr.	Adenoacanthoma	5,000 r	29	3 diam.	Mild, 36th–43rd day	.....	.....
5. 1939. 63 yr.	Caruncle	4,870 r	19	3 diam.	Mild, 26th–40th (?) day	.....	Good. Function good
6. 1944. 68 yr.	Caruncle	5,100 r	19	2.5 diam.	Moderate, 23rd–44th day. Late small necrosis, 3 months	.....	Moderate atrophy. Function good

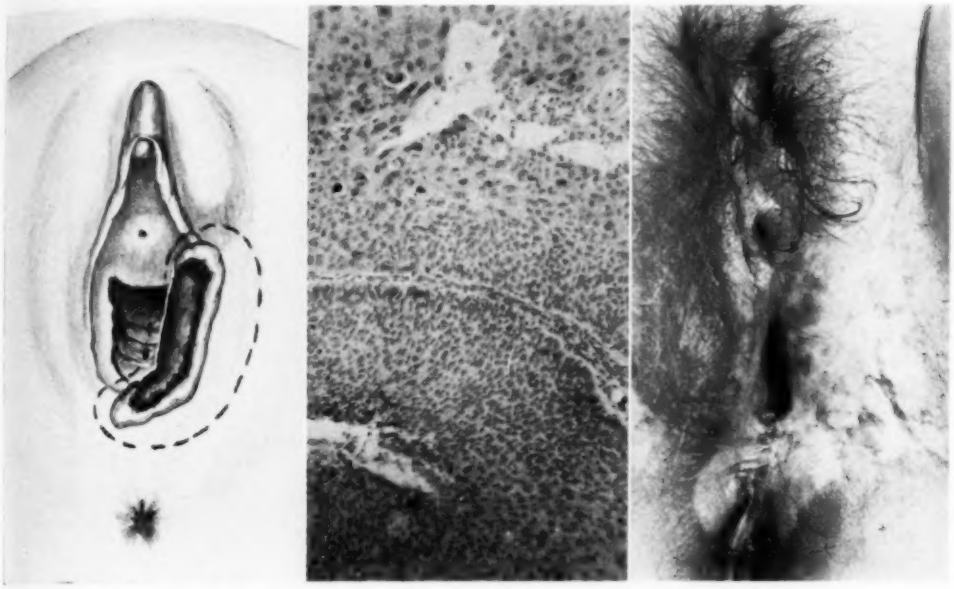
changes are much less disabling than they would have been after surgery for the extensive lesions, even if that had been possible.

It should be noted that in only 2 of the 8 patients had the carcinoma developed on the basis of a vulvar atrophy and leukoplakia. Lesions developing on marked mucosal changes of this type are less favorable for radiation therapy than those arising on an otherwise apparently normal mucosa. Lesions developing in the presence of more diffuse mucous membrane changes would necessitate irradiation of such a large vulvar area that the dose required for sterilization of the carcinoma would not be tolerable. Furthermore, it seems that under these conditions the mucous membranes are even more sensitive to irradiation than normal vulvar mucosa in general. In one patient, not included in this series, we observed such a marked vulvar reaction after a dose of 1,700 r in fifteen days, over a 5 × 7-cm. field, that we were forced to discontinue treatment and to resort to surgery. We therefore feel that in the presence of a general senile atrophy of the mucosa or a more diffuse leukoplakia, vulvectomy is the preferable procedure in the presence of carcinoma.

CARCINOMA OF THE URETHRA

Carcinoma of the female urethra is rare. In 19,000 admissions to the Pondville Hospital during fourteen years only 10 carcinomas of the female urethra and one carcinoma of the male urethra were encountered (Graves and Guiss). During the years 1923 to 1934 there were 17 cases of female urethral carcinoma observed in the New York State Cancer Hospital (Watson), and 2 male urethral carcinomas.

In an evaluation of Watson's results, it is essential to consider the difficulties of the microscopic diagnosis which are sometimes encountered. In 30 per cent of his series a second biopsy was found necessary for correct diagnosis. The diagnostic error may be on either the negative or the positive side. The erroneous diagnoses in Watson's series were infectious granulation tissue, papilloma, and caruncle. In 2 of our own cases that had originally been treated under the diagnosis of carcinoma, a



Figs. 1, 2, and 3. Case 1, Table I: Carcinoma of the vulva after incomplete surgical removal. Fig. 1 (left). April 8, 1940, prior to roentgen therapy. Fig. 2 (center). Epidermoid carcinoma. Fig. 3 (right). Condition of vulva Feb. 20, 1946, six years after roentgen therapy. Treatment: 4,100 r in twenty-one days (April 9 to April 29, 1940), 200 kv., 2 mm. Cu.

later review of the sections led to a correction of this diagnosis to urethral caruncle, and these cases are therefore excluded. They are interesting, however, from the point of view of the late condition of the mucous membrane after heavy irradiation (Figs. 11 and 12).

We have treated 4 cases of true carcinoma of the female urethra with external roentgen therapy directed to one field against the urethral opening, with the beam coinciding with the axis of the urethra. All cases were treated with 200-kv. radiation, 3 of them with 2.0 mm. copper filtration, the last one with 1.0 mm. copper. Three of the tumors were adenoacanthomas, one an undifferentiated epidermoid carcinoma. In addition we have seen 3 carcinomas of the urethra which were so far advanced that treatment was refused. Since this procedure seems to give satisfactory results without intolerable by-effects, we include the clinical data of the 4 cases in detail. In the summarizing table (Table II), we have added the 2 cases of urethral caruncle which were treated on the erroneous diagnosis of carcinoma, because they give us additional information as to the tissue tolerance for this irradiation technic.

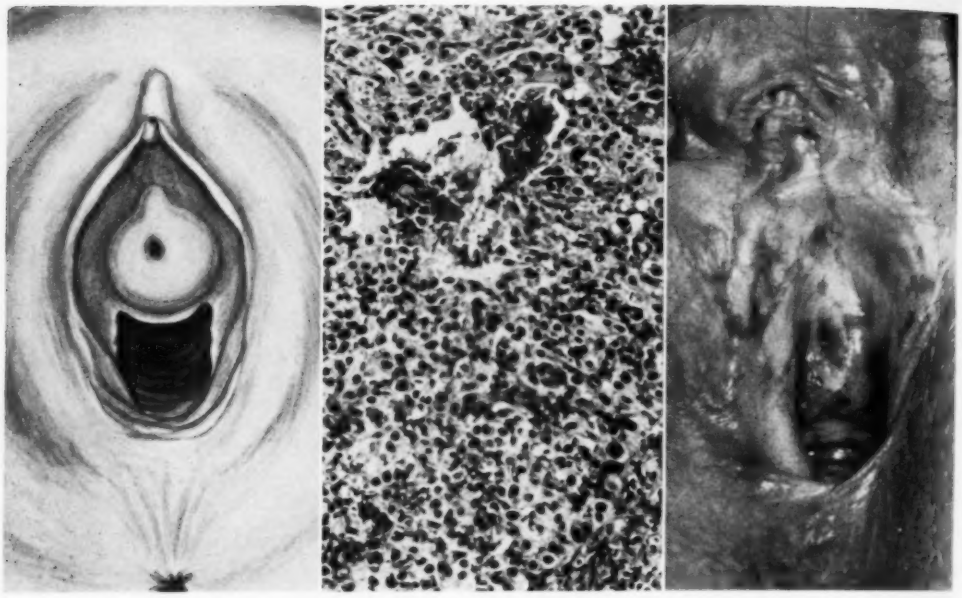
CASE 1: L. B. T., white female, age 61 years, was admitted in September 1942. The pertinent facts of the history were as follows: oophorectomy twenty years previously for ovarian cysts; no menstrual bleeding since then; brownish vaginal discharge for twenty years; no change in type of discharge during the year preceding admission; a lump noticed around the urethra three weeks earlier.

Examination (Fig. 4): Examination showed an area of induration 2.5 cm. in diameter around the external urethral orifice, extending anteriorly to about 0.5 cm. behind the anterior commissure of the minor labia. The depth of induration, by vaginal palpation, was 1.5 cm. The vulvar mucosa overlying the induration was smooth and not ulcerated. There was no obstruction; no pain on urination; no bleeding. No inguinal lymph nodes were palpable.

Biopsy: Epidermoid carcinoma, grade III (Fig. 5).

Roentgen Therapy (Sept. 25 to Oct. 14, 1942): 200 kv.; 2 mm. copper + 1 mm. aluminum; 60 cm. T.S.D.; field size 3.5 and 4.0 cm. diameter; total dose 5,650 r/skin in twenty days.

There was no discomfort throughout the treatment. At the end of the treatment period the tumor had not changed in consistency or size. There were



Figs. 4, 5, and 6. Case 1, Table II: Carcinoma of urethra.
Fig. 4 (left). Sept. 12, 1942, prior to roentgen therapy. Fig. 5 (center). Epidermoid carcinoma, Grade III. Fig. 6 (right). Condition of vulva Oct. 17, 1947, five years after therapy. Treatment: 5,650 r in twenty days (Sept. 25 to Oct. 14, 1942), 200 kv., 2 mm Cu.

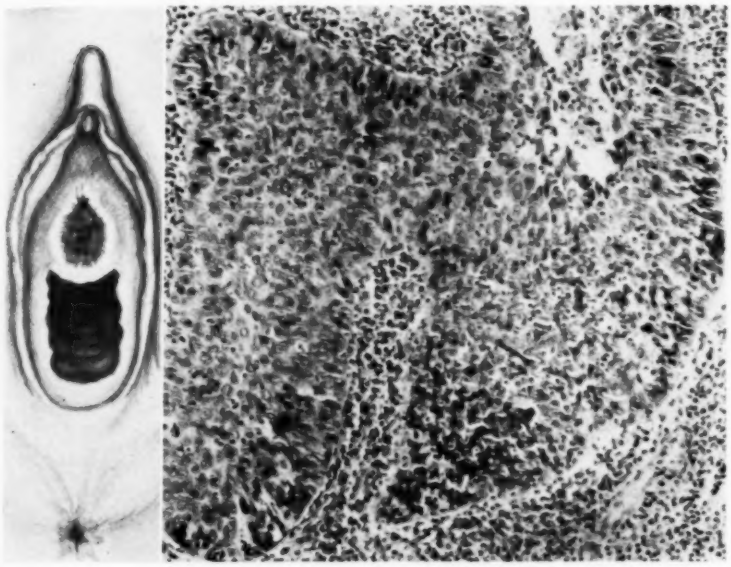
no urinary complaints. On the last treatment day there was slight bleeding from the urethra and some injection over the mucosa, with a small patch of false membrane in the adjoining anterior vaginal wall. During the following week the reaction progressed and on the twenty-fifth day after beginning of treatment a thick membrane was demonstrable overlying the urethral opening itself.

On Oct. 27, 1942, thirty-two days after beginning of treatment, the reaction had developed to such an intensity that hospitalization was required. There was an edema of the urethral opening with bleeding and severe pain on urination. The reaction persisted in this intensity for two weeks and on Nov. 12 necessitated the introduction of an indwelling catheter. During the following week the edema and membrane slowly subsided. On Nov. 28, sixty-four days after beginning of treatment, the mucosa had resumed normal appearance with the exception of a mild edema. At that time the palpable infiltration had entirely disappeared.

On Oct. 27, 1943, one year after treatment, the irradiated area appeared normal on inspection and palpation. There was no subjective discomfort. Two weeks later the patient complained of localized pain. There was a superficial epithelial defect 4 mm. in length and 1 mm. in width in the treatment area. This developed into a localized radiation necrosis less than 0.5 cm. in diameter, with a rather marked surrounding inflammatory reaction and edema of the urethra. The patient was again hospitalized and treated by indwelling catheter, lanolin ointment, and chlorophyll. The catheter was removed after four weeks. At that time the edema and inflammatory reaction had considerably improved. The necrosis itself did not completely heal until the first week of February, two and a half months after it started. The patient was discharged from the hospital on Feb. 7, 1944. At that time the mucosa showed only a moderate atrophy.

Since then there have been no further complications. The patient keeps the area meticulously clean and covered with lubricating ointments. There developed a mild urethral obstruction which necessitates intermittent dilatations. There are moderate atrophy and telangiectasia (Fig. 6).

As we now know, this patient was quite definitely over-treated, receiving a dose beyond the tissue tolerance and probably higher than was necessary to control the tumor. She had a very intense primary reaction necessitating one month's hospitalization, followed one year later by a localized necrosis necessitating almost three months' hospitalization. The tissues by now—after roentgen therapy—show a moderate telangiectasia and atrophy of the mucosa, but the lesion remains controlled and the patient is practically without sub-



Figs. 7 and 8. Case 2. Table II: Adenoacanthoma of urethra, ulcerated lesion. Fig. 7 (left). Aug. 30, 1943, prior to treatment. Fig. 8 (right). Pre-irradiation biopsy. Treatment: 5,200 r in twenty-two days (Sept. 14 to Oct. 5, 1943), 200 kv., 2 mm. Cu. Patient well to date (four years).

jective discomfort, although careful avoidance of infection remains necessary.

CASE 2: L. L., white female, age 57 years, was admitted in September 1943. Hysterectomy had been done eight years earlier for fibroids. There had been no subsequent bleeding until two years ago, when the patient had noticed occasional spotting originating from the urethra. She was treated elsewhere at that time, supposedly for a small tumor, and the bleeding stopped. One month prior to admission she had a major hemorrhage, and since then there had been repeated spotting.

Examination (Fig. 7): Examination showed the urethral meatus to be wide open. A mushy papillary growth was visible in the external opening with some palpable thickening on the posterior urethral wall on vaginal examination. There was no obstruction.

Biopsy: Adenoacanthoma (Fig. 8).

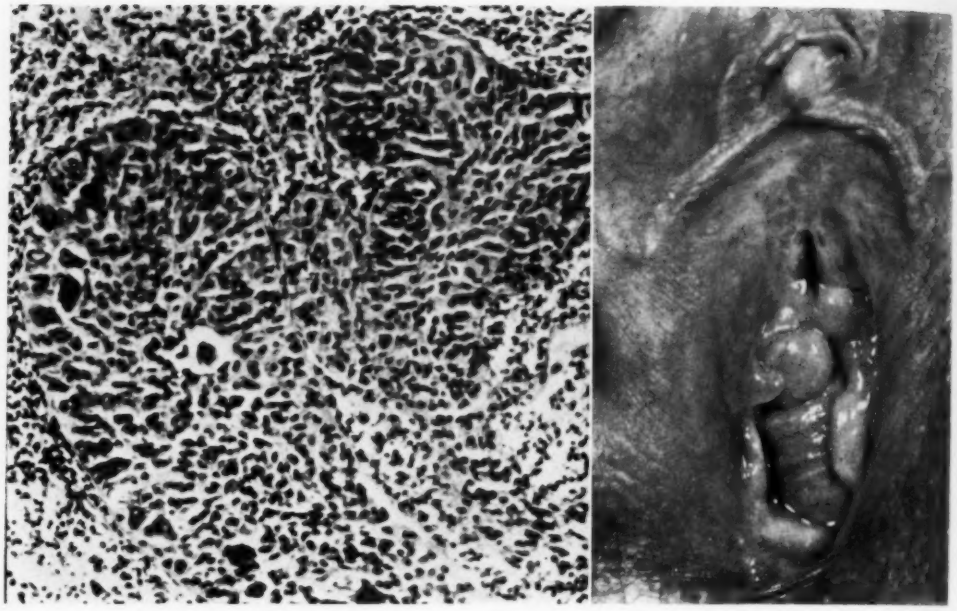
Roentgen Therapy (Sept. 14 to Oct. 5, 1943): 200 kv.; 2 mm. copper + 1 mm. aluminum; 60 cm. distance; field size 3.5 cm. diameter; total dose 5,200 r/skin in twenty-two days.

During the last two treatment days there was a beginning thin membrane covering the external meatus. The patient complained slightly of burning during the last three treatment days. On Oct. 11, twenty-eight days after beginning of treatment, the reaction had reached its height, with a well demarcated false membrane overlying the entire treated area with the urethral opening in the center. There was very little subjective discomfort. On Nov. 3, 1943, fifty-one days after beginning of treatment, the reaction had entirely subsided and there were still slight injection and slight edema around the urethra. There was no subjective discomfort.

In March 1944, six months following therapy, the patient experienced occasional burning in the treated area, and a superficial erosion of the mucosa posterior to the urethral opening became demonstrable. During the following month there developed a superficial necrosis, 4 mm. diameter, extending into the posterior circumference of the urethral opening. Under conservative ambulatory management, this necrosis healed slowly. It was not completely epithelized until September, five months after the beginning of the breakdown. In December 1944, the mucosa showed a very slight atrophy but otherwise was entirely normal, and since that time the treated area has remained soft without evidence of tumor or marked mucosal change.

CASE 3: M. E. I., white female, age 68 years, was admitted Dec. 11, 1945. For about five months she had experienced difficulty of urination, with pain, and at times complete obstruction. Following the discharge of blood clots, obstruction was overcome. She had been treated elsewhere by cautery three months previously.

Examination: Examination showed induration in the posterior urethral wall extending upward for about 3 cm. On inspection a flat ulceration was discovered in the posterior circumference of the urethral wall.



Figs. 9 and 10. Case 3, Table II: Adenoacanthoma of urethra.
Fig. 9 (left). Biopsy prior to treatment. Fig. 10 (right). Condition of vulva Nov. 10, 1947, two years after therapy. Treatment: 4,600 r in thirty-two days (Dec. 18, 1945 to Jan. 8, 1946), 200 kv., 2 mm. Cu.

Biopsy: Adenoacanthoma (Fig. 9).

Roentgen Therapy (Dec. 18, 1945, to Jan. 18, 1946): 200 kv.; 2 mm. copper + 1 mm. aluminum; 60 cm. distance; field size 3 cm. diameter; total dose 4,600 r (skin) in thirty-two days. At the end of treatment there was no demonstrable reaction. During the last few treatment days there was a slight complaint of occasional burning, mainly during urination, with some bleeding on urination; no sign of obstruction. On Jan. 23, 1946 (37th day), there was a beginning false membrane overlying the inner surface of the minor labia and the mucosa surrounding the urethra. The reaction reached its height in two days and began to subside after four days. On Feb. 1, 1946, forty-six days after beginning of treatment, the reaction had completely disappeared. There was a moderate injection of the mucosa.

One month after treatment, the patient complained of some incontinence, of the type of an overflow bladder. This has persisted throughout the following observation time to date. We have never been able to determine the mechanism of this type of incontinence. It is obviously not due to a scarry obstruction because a dilatation to French No. 20 was done with no difficulty but without any improvement. Examination by two urologists failed to reveal the mechanism and they could not suggest any therapy other than the use of an indwelling catheter for cleanliness. With the exception of the incontinence, patient is in good condition, the mucosa appears normal and there is no sign of tumor at this time, almost two years after treatment (Fig. 10).

CASE 4: M. W., white female, age 65 years, was admitted April 17, 1947, with a history of bleeding from the urethra for two months without pain and without signs of obstruction. Six months prior to admission, part of a tumor was removed elsewhere, with prompt recurrence.

Examination: There was an ovoid raised node, 1 × 1.5 cm., *at the junction of the vulvar mucosa with the right circumference of the external urethral orifice.* The tumor was well demarcated and raised about 2 mm. The overlying mucosa was intact. The anterior vaginal wall was perfectly soft.

Biopsy: Adenoacanthoma.

Roentgen Therapy (April 22 to May 20, 1947): 200 kv.; 1 mm. copper + 2 mm. aluminum; 60 cm. distance; field 3 cm. in diameter; total dose 5,000 r (skin) in twenty-nine days.

During the fourth treatment week there was slight urinary frequency with discomfort during urination. Thin patches of false membrane appeared on May 27, 1947—the 36th day after the beginning of treatment. During the following days this developed into a well localized membranous reaction which reached its height on May 31 and had almost disappeared on June 3, forty-three days after beginning of treatment. On June 10, 1947, the mucosa showed only slight injection. There was, however, still an indurated ridge at the site of the former palpable lesion. On July 4, 1947, the inflammation had com-

pletely disappeared. To date, no recurrence is demonstrable and the mucosa appears normal.[1]

From the experience with this small number of cases we would conclude that a total dose of around 5,000 r (skin) in about twenty-five days is tolerated by the mucous membrane for the small fields necessary for this type of lesion and is apparently sufficient for sterilization. In none of the cases treated with doses in the neighborhood of

Fig. 11. Case 5, Table II: Urethral caruncle, treated under the erroneous diagnosis of carcinoma, Feb. 28, to March 18, 1939 (4,870 r in nineteen days, 200 kv., 2 mm. Cu). Condition of mucosa Sept. 11, 1946, seven and a half years after treatment.

5,000 r was there any intolerably severe reaction or any late damage as far as we can yet determine that would jeopardize the usefulness of the procedure. The reactions in these cases developed late, after the end of treatment, and therefore cannot be used as a guide for the conduct of therapy itself. The earliest reaction observed was around the twenty-third day. In two cases the reaction did not start before the thirty-sixth day after the beginning of treatment. The reaction had not completely subsided until around the fortieth to forty-sixth day. In none of these cases was there a sufficiently severe initial reaction to interfere with adequate drainage of the bladder.

[1] After this paper was prepared, two nodules developed, one in the suprapubic skin and one in the left major labium. These were excised and the histology corresponded to the original findings. The treated urethral area has remained unchanged for one year.

Fig. 12. Case 6, Table II: Urethral caruncle, treated under erroneous diagnosis of carcinoma, Jan. 10 to Jan. 28, 1944 (5,100 r in nineteen days, 200 kv., 2 mm. Cu). Condition of mucosa Aug. 22, 1946, two and a half years after treatment.

That a dose of 5,000 to 5,200 r is the upper limit of tolerance, we would conclude from the experience with Case 1, in which 5,650 r were given in twenty days. The dose was carried to this level because, by the end of treatment, the tumor was completely unchanged and no sign of beginning reaction was observed. At the time this treatment was given, we did not have sufficient experience to realize the late appearance of the reaction in this location. This patient had an unusually heavy reaction with a severe edema of the urethra at times necessitating the use of an indwelling catheter and requiring hospitalization for about one month. One year after the treatment she had a small radiation necrosis which again necessitated hospitalization for almost three months. A mild stricture also developed, which still requires intermittent dilatations, although by now, five years after treatment, there is no other disability. We would, however, believe that such a dose is higher than necessary and should be avoided. *Three patients treated are so far free of demonstrable disease for periods of five years, four years, and two years, respectively.* The fourth patient was treated only recently. None of these patients had any treatment to the

lymphatic area. The late tissue changes incident to irradiation are shown in Figures 10, 11, and 12.

From the experience presented we feel justified in concluding that external roentgen therapy in the 200-kv. range is able to control reasonably early carcinoma of the female urethra with better functional results, less initial morbidity, and less serious late sequelae than surgery or interstitial irradiation, provided the cases are carefully selected and the treatment itself, as well as the management of the primary reaction, is conducted with skill and close attention to minute details.

SUMMARY

1. External roentgen therapy with 200-kv. radiation for the treatment of the primary lesion of carcinoma of the female urethra and of the vulva is discussed.

2. Four carcinomas of the female urethra were treated. Three patients are well to date for periods of five years, four years, and two years, respectively. The fourth patient was treated only recently.

3. Eight cases of carcinoma of the vulva outside of the periurethral area and too far advanced for radical surgery were treated. Five are well seven years, four and a half years, two and a half years, two and a half years and one and one-quarter years, respectively. Three are dead, all of them from metastases.

4. Doses up to about 5,000 r measured on the skin, over a period of about twenty-five days, were found to be tolerated by the mucous membrane for the small fields of 3 to 3.5 cm. diameter necessary for the treatment of early urethral carcinomas and sufficient for their sterilization. The reactions from this treatment are not out of proportion to the functional and anatomical results obtained. Doses beyond this amount may lead to such intense reactions as to make the usefulness of the procedure questionable and, as far as can be judged, are not necessary for sterilization of this type of tumor. For the less differentiated tumors of the vulva, smaller doses (4,000 to 4,500 r in twenty to twenty-six days) are sufficient and, therefore, large inoperable lesions can still be successfully treated without intolerable mucosal damage.

5. We feel that roentgen therapy has an indication for the treatment of fairly early carcinoma of the urethra and for advanced carcinoma of the vulva beyond surgical approach. For earlier carcinomas of the vulva outside of the periurethral area, surgical excision is probably the simpler procedure. Carcinomas developing in a very atrophic mucosa or in the presence of leukoplakia, regardless of size, are unfavorable for radiation therapy and are better treated surgically.

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SUMARIO

Roentgenoterapia del Carcinoma de la Uretra Femenina y la Vulva

1. Discútese la roentgenoterapia con 200 kv. de irradiación en el primario carcinoma de la uretra femenina y la vulva.

2. Tratáronse cuatro casos de carcinoma de la uretra femenina. Tres de las enfermas han continuado bien hasta la fecha por períodos de cinco, cuatro y dos años, respectivamente. La cuarta enferma fué tratada hace muy poco tiempo.

3. Tratáronse ocho casos de carcinoma de la vulva fuera de la zona periuretral y demasiado avanzados para cirugía radical. Cinco se hallan bien a los siete años, cuatro años y medio, dos años y medio, dos anos y

medio y año y tres meses, respectivamente. Tres enfermas han muerto, todas de metástasis.

4. Dosis hasta de unos 5,000 r medidos en la piel, durante un período de 25 días, fueron toleradas por la mucosa en los pequeños campos de 3 a 3.5 cm. de diámetro necesarios para el tratamiento de los carcinomas uretrales incipientes, resultando suficientes para esterilizarlos. Las reacciones a este tratamiento no fueron desproporcionadas a los resultados funcionales y anatómicos obtenidos. Dosis mayores pueden ocasionar reacciones tan intensas que pongan en tela de juicio la utilidad del procedimiento, y en lo que cabe juzgar, no son necessarias para esterilizar los tumores de este género. Para los tumores menos diferenciados de la vulva, dosis menores (4,000 a 4,500 r en 20 a 26 días) son suficientes, y por lo tanto, todavía pueden tratarse con éxito grandes lesiones inoperables sin lastimar intolerablemente la mucosa.

5. La roentgenoterapia tiene su indicación en el carcinoma bastante temprano de la uretra y en el carcinoma avanzado de la vulva inabordable con la cirugía. En los carcinomas más tempranos de la vulva fuera de la zona periuretral, la excisión quirúgica constituye probablemente el procedimiento más sencillo. Independientemente de su tamaño, los carcinomas que se desarrollan en una mucosa muy atrofiada o en presencia de leucoplaquia no se prestan para la radioterapia y es mejor tratarlos quirúrgicamente.

Carcinoma of the Endometrium

Measurements of the Radiation Distribution Around Various Multiple Capsule Applications of Radium in Irregular Uteri[1]

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A COMPARISON of the radiation distribution with several methods of radium application for the treatment of carcinoma of the endometrium was made from the results of an earlier experiment (8). It was concluded from that study that the multiple-capsule packing method described by Heyman (5) was superior from the standpoint of the resultant radiation fields. The experimental conditions described, however, necessarily excluded many variables encountered in practice which must be taken into consideration in order to achieve a basis for more accurate comparison. In discussion of the study, Dr. E. H. Quimby and Dr. James Heyman both suggested that more practical aspects of the multiple-capsule method be further explored. Its adaptability to uteri varying in size and shape was the specific problem brought out, and to that question the present study is devoted.

Many years ago Sampson emphasized the variations in the size and shape of uteri containing endometrial carcinoma (10). The configuration of the endometrial cavity may become distorted by the growth of the carcinoma itself or as a result of concomitant benign conditions. Among the latter, myomata are frequent offenders. The incidence of myomata in conjunction with carcinoma of the endometrium has been stated by several authors to be about 30 per cent, although there is little evidence to indicate an actual etiological relationship between the two conditions (11). The usual figure given for the incidence of myomata in women over thirty years of age, in autopsy material, is 20 per cent (9).

Sampson further pointed out the technical difficulties which variations in the size and shape of the uterus may cause in the effective intrauterine application of radium. Distortion of the cavity may cause the sources to be displaced away from small tumors, or large tumors themselves may deflect the intracavity sources from the bases and actively growing portions of the neoplasm. There is danger of rupture of the uterus in the presence of such distortion and irregularity. Also, endometrial carcinoma is a post-menopausal disease and may occur in atrophic uteri. Achieving a uniform field of radiation under such conditions, where only a few sources can be used, is not an easy matter. Furthermore, introduction of radium sources into these small cavities with fibrotic walls and a stenosed canal is a difficult and potentially dangerous procedure.

Since it is difficult, even after examination under anesthesia and dilatation and curettage, to outline the exact size and configuration of some of these tumors, the variations become important. Theoretically, the multiple-capsule method of radium implantation, which utilizes as many small sources as are needed to fill the available space, best adapts itself to the variations in the geography of the endometrial cavity. Whether this adaptability acts toward uniformity of radiation distribution is a question of practical importance.

The purpose of the experiment to be described here was to simulate the abnormal conditions one might expect to encounter in the radium treatment of carcinoma of the uterine corpus, and from a study of the radiation distribution with typical examples of complicated applica-

[1] From the Edward Mallinckrodt Institute of Radiology; and the Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Mo. Presented at the Thirty-third Annual Meeting of the Radiological Society of North America, Boston, Mass., Nov. 30–Dec. 5, 1947.

tions to outline the limitations of the multiple-capsule method of treatment, again upon the basis of distribution of radiation.

EXPERIMENTAL PROCEDURE

For the experimental study, the film method of dosimetry, described in the previous investigation, has again been used. There have been some variations, however, from the original procedure necessitated by the nature of the experimental applications.

Uteri were obtained after hysterectomy for benign conditions and four of these were selected because they showed typical variations from the normal. The first was excised by vaginal hysterectomy for prolapse. The corpus was regular but atrophic, and the cervix was hypertrophied. The endometrial cavity was regular but narrowed in the region of the fundus. The second contained a single large intramural myoma which distorted the endometrial cavity into a crescent shape, although the cavity itself was small. The third contained many intramural myomata and was enlarged; the cavity was spacious and regular. The fourth, too, was myomatous; the cavity was enlarged and distorted by intramural myomata. These four uteri represent the extreme situations which may be expected; namely, a small regular cavity, a small irregular cavity, a large regular cavity, and a large irregular cavity.

In the fresh state these excised uteri were packed with radium capsules in the same manner as *in vivo* (7). The cervix was held by a tenaculum and the cervical canal was dilated instrumentally. The capsules usually used in treatment were packed into the uteri with the regular instrument devised for this purpose. There were fifteen capsules available:

(*a*) Six small capsules; 0.5 cm. diameter, 1.5 cm. external length, 5 mg. Ra/ea.

(*b*) Six intermediate capsules; 0.5 cm. diameter, 2 cm. external length, 10 mg. Ra/ea.

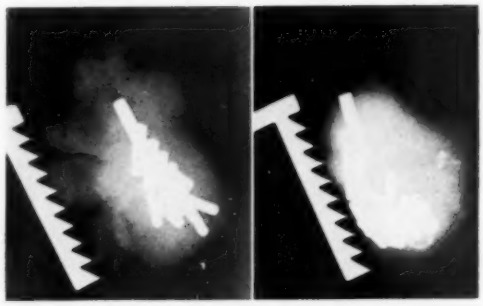


Fig. 1. Roentgenograms, anterior-posterior and lateral projections, of an excised myomatous uterus packed with radium capsules.

(*c*) Three large capsules; 0.7 cm. in diameter, 2 cm. external length, 20 mg. Ra/ea.

The smallest capsules were placed in the fundus of the uterus first and maneuvered with the packing instrument to conform to the configuration of the cavity. Then the longer capsules of the small diameter were introduced, and finally the widest capsules were packed into the cervical canal. In the case of the two small uteri—11 capsules were used (6 small and 5 intermediate), but in the others all 15 capsules were necessary to fill the available space.

The capsules used here were the same as those described in the previous experiment, but the radium sources which they contained were different because of a change in the radium supply. These were as follows:

No. 25; 1 mg. cells, 5 mm. gold filter, 1.0 cm. active length.

No. 6; 1 mg. tubes, 5 mm. Pt filter, 1.7 cm. active length.

No. 3; 20 mg. tubes, 5 mm. Pt filter, 1.7 cm. active length.

Anterior-posterior and lateral radiographs were taken after the cavities were packed with the capsules to determine their spatial distribution. In order to facilitate reproduction of the radiographs to scale, a centimeter notched ruler was placed along the mid-plane of the uterus in either view (Fig. 1). From these radiographs diagrams were made of the uterine outlines and the intrauterine capsules.

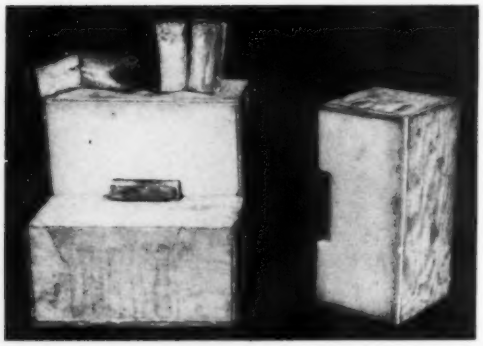


Fig. 2. Paraffin phantom used for experimental studies.

Another variation from the former experiment was in the choice of phantom material. Because a more pliable medium than Presdwood was needed to reproduce the configurations of the radium sources to be studied, paraffin was selected. There are, of course, differences in the scattering characteristics of the two materials (12), but these differences are not great when dealing with gamma rays.

A large block of paraffin (20 cm.) was cut along the horizontal and vertical planes into quarters and a notch, $2 \times 2 \times 9$ cm., was excised from each central border. Interchangeable blocks of paraffin were then made to fit the central cavity formed when the larger blocks were approximated. These smaller blocks were cut in the horizontal plane and were hollowed out to receive the radium capsules according to the configurations shown in the radiographs of the packed uteri for each condition to be studied. With this set-up it was possible to rebuild the phantom with sheets of film through the center and around the radium sources in the horizontal and vertical planes, or the coronal and sagittal planes, in relation to the uterus (Fig. 2).

The film used was again Defender Adlux, and all sheets were of the same emulsion number, coming from the same box. Film sheets, 8×10 inches, were cut to size in the darkroom and covered with two layers of black paper. Pin pricks through the paper were used as orientation points in relation to the radium sources for future reference.

Exposures equivalent to 1,000 mg. hr. with 0.5 mm. Pt filter were made for each of the four irregular multiple capsule applications plus a three-tube tandem (5.1 cm. active length) in the phantom. A calibration film was exposed in air to a small source (25 mg., 1.0 cm. active length, 0.5 mm. Pt).

All of these films were developed together under standard conditions in Dectol at 68° F. for three minutes. The procedure was done by hand agitation in a pan under carefully controlled conditions. After drying, the films were marked with soft lead pencil to show reference points and grid lines. The films could then be read on a Marshall transmission densitometer.

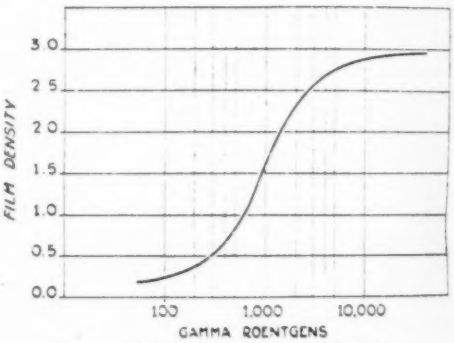


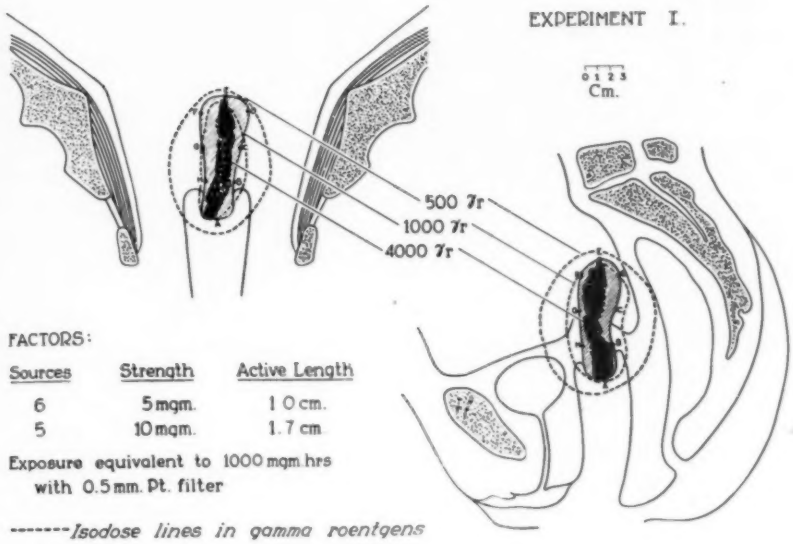
Fig. 3. Calibration curve for Adlux film.

The calibration curve used in these experiments is shown in Figure 3 and is the typical characteristic darkening curve for this film. It was constructed from published tables for radiation from radium sources (2).

RESULTS

The results of the experiments are shown in Figures 4 to 7, inclusive. These diagrams indicate the shape of the mass of capsules assumed in each case, the size and shape of the uteri, and the relationships between these organs and the normal pelvic structures. Certain points on the periphery of each uterus in both planes are indicated by the letters *A* to *G*, which will be referred to later. The isodose curves indicated are those for 500, 1,000, and 4,000

RADIATION DISTRIBUTION THROUGHOUT PELVIS WITH MULTIPLE CAPSULE RADIUM IMPLANTATIONS IN IRREGULAR UTERI



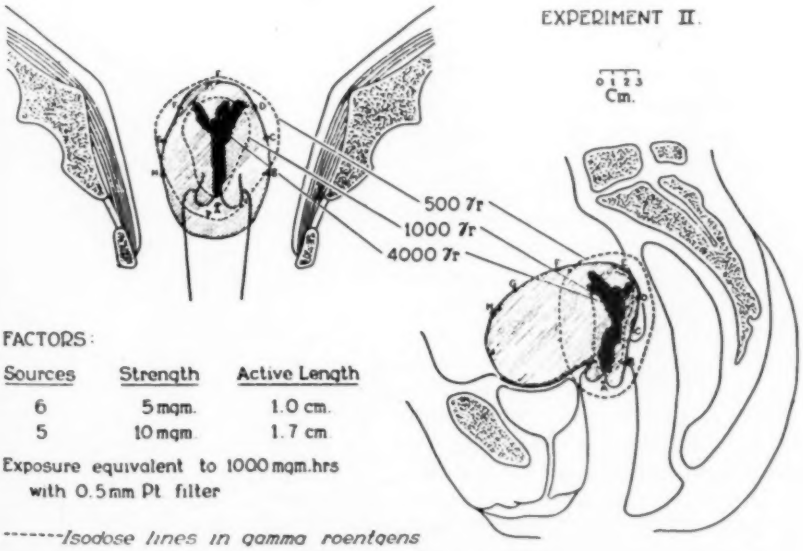
FACTORS:

Sources	Strength	Active Length
6	5 mgm.	1.0 cm.
5	10 mgm.	1.7 cm

Exposure equivalent to 1000 mgm.hrs with 0.5 mm. Pt. filter

-------*Isodose lines in gamma roentgens*

RADIATION DISTRIBUTION THROUGHOUT PELVIS WITH MULTIPLE CAPSULE RADIUM IMPLANTATIONS IN IRREGULAR UTERI



FACTORS:

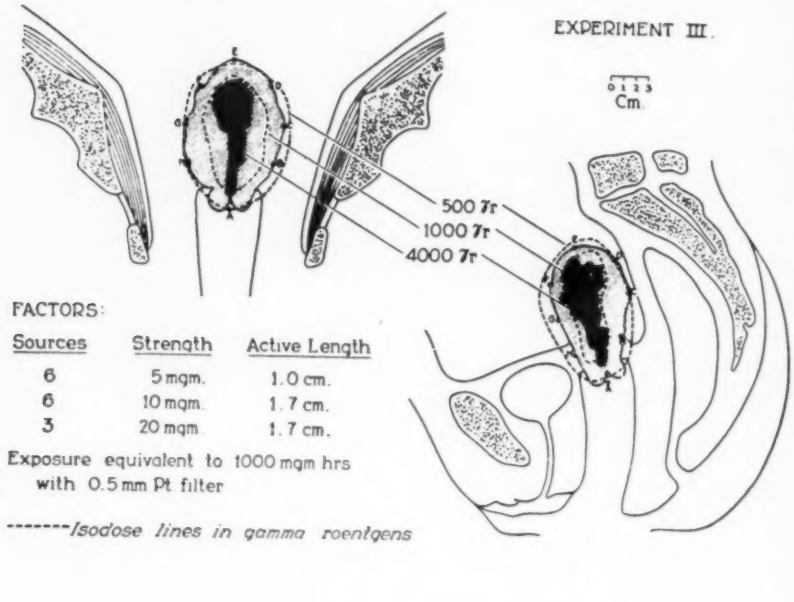
Sources	Strength	Active Length
6	5 mgm.	1.0 cm.
5	10 mgm.	1.7 cm

Exposure equivalent to 1000 mgm.hrs with 0.5 mm Pt filter

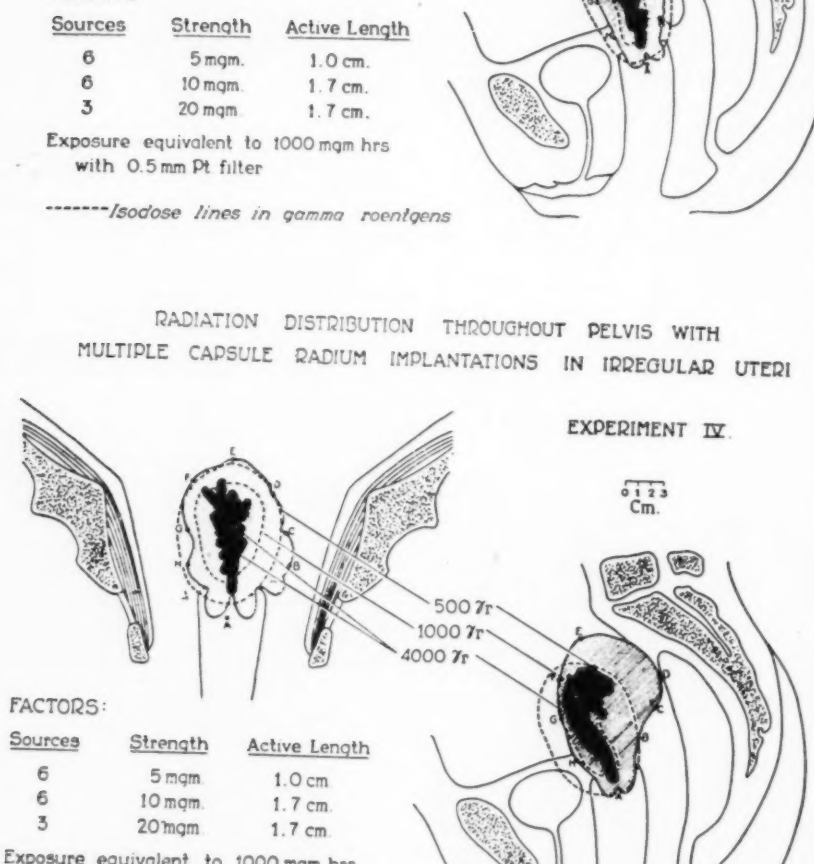
-------*Isodose lines in gamma roentgens*

Figs. 4 and 5. Experiments I and II.

RADIATION DISTRIBUTION THROUGHOUT PELVIS WITH MULTIPLE CAPSULE RADIUM IMPLANTATIONS IN IRREGULAR UTERI



RADIATION DISTRIBUTION THROUGHOUT PELVIS WITH MULTIPLE CAPSULE RADIUM IMPLANTATIONS IN IRREGULAR UTERI



Figs. 6 and 7. Experiments III and IV.

gamma roentgens, assuming a 1,000 mg.-hr. exposure for each application. These were chosen because they represent the extremes of the straight portion of the calibration curve.

In general the diagrams indicate that the field of radiation naturally follows the conformation of the mass of intracavity capsules and that this mass is quite similar in shape to the uterus itself. In Experiment I it is seen that the narrowed fundus due to atrophy causes the capsules to assume a form similar to the tandem and that the radiation field is limited to a certain extent. With the small irregular cavity shown in Experiment II, the periphery of the uterus is quite distant from the mass of capsules on one side; therefore, the amount of effective radiation falling throughout the uterus is uneven. Experiment III represents the most ideal conditions for multiple capsules in that the cavity is both regular and large. Here the fields of radiation are wider and more uniform than in the others. Experiment IV, which has the advantage of a large cavity, shows again the disadvantage of the eccentric placement of the capsules, the effect being similar to that in Experiment II.

Aside from the general observations shown by the diagrams, it is necessary to present some data upon which concrete comparisons may be made. For this purpose, Table I has been prepared. Here values are given in gamma roentgens per 1,000 mg.-hr. exposure, for the doses falling on the periphery of the uteri at specific points in the mid-coronal and mid-sagittal planes. These points are indicated in the diagrams as:

A. The external os
B. The level of the internal os, right
C. The level of the mid-corpus, right
D. The level of the cornu, right
E. The mid-point of the fundus
F. The level of the cornu, left
G. The level of the mid-corpus, left
H. The level of the internal os, left.

The values obtained with the multiple-capsule arrangements are compared to similar ones which would fall at the same points if a three-tube tandem of 5.1 cm. active length were placed in the uterus for an equal mg.-hr. exposure as shown. From the table one can see that there is a wider variation of values at the various points with the tandem measurements than with the multiple capsule measurements. Also the tandems show the point of greatest dosage to be at the level of the internal os and the point of lowest dosage to be the level of the fundus. With the multiple capsules these points vary because of the more irregular spatial placement of the sources.

If we assume that uniformity of the field of radiation around any application of radium is desirable, we can judge these various plans of treatment from that point of view. Table II has been constructed from the data presented in Table I and indicates the values for doses falling at the points of minimum and maximum intensity for the four experimental conditions with tandem and multiple-capsule applications. The difference between the two values gives a measure of uniformity for comparison. We can see from the third column ("uniformity as measured by range of dosage") that the multiple-capsule arrangement is superior to the tandem in each instance. The least difference between the two methods is with the conditions of Experiment I, where the multiple capsules assume a tandem shape; the greatest difference is with the conditions of Experiment III. Further, to show the effect of uniformity on the possible mg.-hr. exposure for each treatment method, the right hand portion of Table II has been prepared. The doses at the points of minimum and maximum intensity limit the possible exposure because the amount at the highest point must not exceed that which may cause general tissue necrosis and deleterious effects; on the other hand, the dose at the point of lowest intensity must not be below that which will control the tumor cells (7). If we consider 7,000 gamma roentgens as the dose necessary to cause death of all the cancer cells, we can express the factor K in

DOSES IN GAMMA ROENTGENS FALLING AT SPECIFIC POINTS ON THE SURFACE OF FOUR EXPERIMENTAL UTERI WITH TANDEM AND MULTIPLE CAPSULE RADIUM TREATMENT METHODS

Experiment	Method 1000 mg-hrs	Plane	Ext. Os A	Int. Os (right) B	Corpus (right) C	Cornu (right) D	Fundus E	Cornu (left) F	Corpus (left) G	Int. Os (left) H
I cavity small, regular	3 sources Tandem	A-P	1100	3000	1800	500	380	550	2300	3000+
		Lat.	1100	3200+	3000	520	350-	560	1600	2300
	11 sources Multiple Capsules	A-P	810	2500	1555	640-	680	700	1000	1200
		Lat.	810	2700+	1700	1180	680	820	1550	1500
II cavity small, irregular	3 sources Tandem	A-P	1100	620	600	540	350	540	600	610
		Lat.	1100	2300	2400+	950	450	350	260	250-
	11 sources Multiple Capsules	A-P	580	420	550	750	540	880+	510	370
		Lat.	700	810	820	860	705	400	210	200-
III cavity large, regular	3 sources Tandem	A-P	1100	760	480	300	200-	320	540	800
		Lat.	1100	1700+	600	340.	280	450	900	1600
	15 sources Multiple Capsules	A-P	450	640	600	580	550	600	550	540
		Lat.	400-	700	480	480	550	640	650	700+
IV cavity large, irregular	3 sources Tandem	A-P	1100	530	960	320	180-	280	540	760
		Lat.	1100	1200+	530	340	180	340	660	1150
	15 sources Multiple Capsules	A-P	500	310	450	450	320	450	700	610
		Lat.	620	500	320	210-	220	680	1000+	900

+ = Point of Maximum Dosage - = Point of Minimum Dosage

Exposures equivalent to 1000 mg-hrs with 0.5 mm. Pt. filter

Table I

the table as 7,000 divided by the dose at the point of minimum intensity. It would then be necessary to multiply the exposure time (1,000 mg. hr.) by this factor to achieve a cancericidal dose at all points on the periphery of the uterus. When this is done, the value at the point of maximum intensity rises by the same factor and should not be above a level which will cause general necrosis, in order to be safe. Table II shows that for the multiple capsule arrangement the factor K is less in each instance, and the resultant dose at the point of maximum intensity is also less, than for the tandem. However, if we consider 15,000 gamma r as the dose beyond which necrosis might occur, none of the resultant values is safe except that in Experiment III with multiple capsules.

Conversely, if we take the value at the point of maximum intensity and express the factor by which the mg.-hr. exposure may be safely multiplied as K^1 (or 15,000/max.), we find that the values for the multiple-capsule applications are higher in each instance than the values for the tandem applications. Again, only in Experiment III does this value approach 7,000 gamma r or the dose necessary to be cancericidal at all points.

A practical measure of the uniformity for each of the plans of application can then be further expressed as the difference between the factors K and K^1. In the table this number approaches unity only in the case of multiple capsules in Experiment III. In the other experiments this difference is less for the multiple capsule applications than for the tandems under the same experimental conditions.

From the applications of these arithmetical tests to the results of the experiments, we can conclude that the multiple-capsule methods adapt themselves fairly

UNIFORMITY OF RADIATION FALLING ON SURFACE OF EXPERIMENTAL UTERI AND ITS EFFECT

Experiment	Treatment Method	Uniformity as measured by range of dosage			Range of dosage as it would effect possible mg-hr exposure				
		Dose at point of minimum intensity	Dose at point of maximum intensity	Difference between minimum and maximum doses	Effect of increasing dose at point of minimum dosage to effective level		Effect of increasing dose at point of maximum dosage to limit of safety		Effective measure of uniformity
NUMBER	EXPOSURE 1000 MGHR	MAX	MIN	MAX-MIN	7000/MIN K	RESULTANT K x MAX	15,000/MAX K'	RESULTANT K' x MIN	K - K'
I	Tandem	3200	350	2850	20.0	64,000	4.7	1645	15.3
	Multiple Capsules	2700	640	2060	11.0	29,760	5.5	3520	5.5
II	Tandem	2400	200	2200	35.0	84,000	6.3	1260	28.7
	Multiple Capsules	880	200	680	35.0	30,800	17.0	3400	18.0
III	Tandem	1700	200	1500	35.0	59,500	9.0	1800	26.0
	Multiple Capsules	700	400	300	18.0	12,600	21.0	8400	- 3.0
IV	Tandem	1200	180	1120	37.0	44,400	12.5	2250	24.5
	Multiple Capsules	1000	210	890	33.0	33,000	15.0	3150	18.0

DOSES IN GAMMA ROENTGENS

Table II

well to the abnormal situations studied. The fields of radiation from these applications can be said to be superior to those around tandems under the same conditions, so far as uniformity is concerned. However, comparison among the results from the multiple capsules themselves show that there are definite limitations in the uniformity of radiation imposed upon the method by irregularities in the shape of the uterus.

A further consideration of the peripheral dose in irregular uteri irradiated by the multiple-capsule method is demonstrated in Table III. Here the average values for the radiation falling in certain planes previously described is shown for each experimental situation. The first column shows the over-all average and may be compared to the values found in similar studies. Benner, by ionization chamber measurements in air, arrived at a figure of 633 r/1,000 mg. hr. on the periphery of normal uteri with the method described by Heyman (3). A value of 700 r/1,000 mg. hr. on the periphery of a normal uterus was obtained in the earlier experiment using this film method of dosimetry for a similar plan of multiple-capsule application. Benner, however, also measured the intensity of radiation around irregular cavities in two instances, one of hour-glass shape and one thin and elongated. For the first condition he found the intensity of radiation 15 per cent less than in the normal uterus, and for the second, 30 per cent less than in the normal uterus. The intensities would thus be 538 r/1,000 mg. hr. and 437 r/1,000 mg. hr. in these cases, which compare favorably with the values found in Table III. Only in experimental Condition I are the values higher than in the normal uterus, because of the thin uterine wall and proximity of the sources to the

AVERAGE DOSES IN GAMMA ROENTGENS FALLING ON SURFACE OF EXPERIMENTAL UTERI AT VARIOUS PLANES

Multiple Capsules 1000 mg.hrs	Average Dose to Periphery of Uterus	Transverse Planes					Median Coronal Plane	Median Sagital Plane
		External Os	Internal Os	Mid-Corpus	Cornua	Fundus	A-P	Lat.
	γr	γr	γr	γr	γr	γr	γr	γr
Experiment I	1251	810	1975	1450	835	680	1136	1367
Experiment II	578	640	450	522	710	622	568	588
Experiment III	569	425	645	570	575	550	564	575
Experiment IV	506	560	580	617	447	270	474	556

Table III

periphery. There is fair correlation among these values. It must be remembered that the measurements of Benner were made under different experimental conditions than the present study. Moreover the experiment which did utilize the same film method of dosimetry as the present one was done in a Presdwood phantom with different radiation sources.

Table III also shows the average values of the doses falling at the periphery of the uteri through several different planes. In Condition I there is greater variation in the various transverse planes than in the other conditions, which do show good uniformity.

Attention was directed to the distribution of radiation in the transverse plane through the mid-corpus for each of the experimental uteri, and the results are presented in Figure 8. This graph shows the variation in range of dosage plotted against distance from the mid-line in the anterior posterior projection for each situation. The mg.-hr. exposure for each of these applications was calculated for 5,000 mg. hr. For comparison, the same values for a tandem application at 3,000 mg. hr. in a uterus of normal size are shown. The positions occupied by the uterine wall, the proximal parametrium, and the adnexa in the normal situation are shown. Also indicated are certain arbitrary levels of radiation which may be considered important from a biological point of view (8). These are 4,000, 7,000, 15,000, and 20,000 gamma roentgens and they are presented to indicate the levels which should cause slight tumor control, good tumor control, possible necrosis, and general necrosis, respectively.

From a study of this graph, one can see that even in abnormally shaped uteri the fields of radiation for the multiple capsule applications are superior to those from a tandem in the normal situation, because a higher mg.-hr. exposure may be allowed and the resulting field of effective radiation is wider.

DISCUSSION

In the consideration of these results one must again be careful to realize that the experimental conditions were limited and

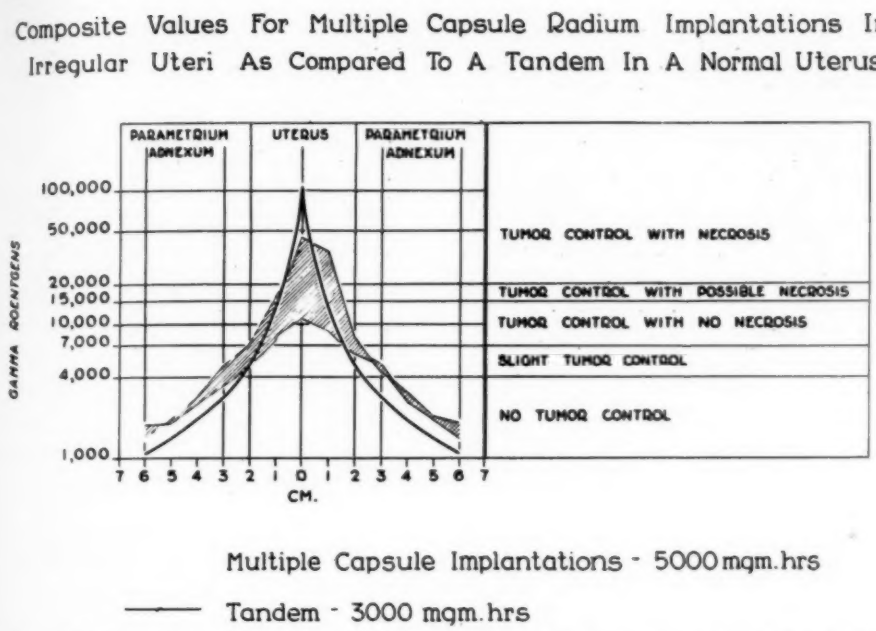


Fig. 8. Radiation distribution lateral to the mid-line of the pelvis along a transverse plane at the level of the mid-corpus.

that there may be further variables to be considered than those here proposed. Studies such as this, which are directed toward problems of radiation distribution under *in vitro* conditions, must necessarily exclude biological variations, which can be most important. Yet there is the natural tendency to interpret these results upon the basis of expected biological responses. As the experimental conditions are made to approach the complicated practical problems, more variables must be considered and the exactitude of these interpretations may decrease. Although any method of treatment must be judged upon its success or failure in actual practice, it is helpful to have experimental evidence of theoretical advantages upon which to justify changes in methods of treatment. With such considerations in mind we can interpret the results of these experiments.

Irregularities in the size and shape of the uterus exert a general deleterious effect upon the effectiveness of multiple-capsule implantations of radium for the treatment of endometrial carcinoma. However, this effect is not so great for the multiple-capsule method as it is with the tandem method of treatment. In other words, the packing technic tends to minimize the disadvantages imposed upon intrauterine radium treatment by such uterine irregularities. There is, then, a greater possibility of achieving an effective result from such radium treatments. The results of treatment by this technic as described by Heyman (4, 6) and others (1) indicate its superiority from a clinical standpoint.

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SUMARIO

Carcinoma del Endometrio. Mediciones de la Distribución de la Irradiación Alrededor de las Cápsulas Múltiples de Radio Aplicadas en Úteros Irregulares

Ya se había observado que la técnica de Heyman de atestar el útero con cápsulas múltiples era, desde el punto de vista de los resultantes campos de irradiación, la más efectiva para aplicar el radio en el cáncer del endometrio. Ahora se ha estudiado la adaptabilidad de dicha técnica a los úteros de varios tamaños y formas, usando para ello cuatro úteros procedentes de histerectomías por estados benignos y que representan los extremos que pueden encontrarse en la práctica, a saber: una cavidad pequeña regular, una cavidad pequeña irregular, una cavidad grande regular y una cavidad grande irregular.

Si bien es cierto que las condiciones de la experimentación fueron limitadas y que en la práctica tal vez haya que considerar importantes variaciones biológicas, es posible interpretar el resultado en el sentido de que las irregularidades en el tamaño y forma del útero ejercen un efecto general adverso sobre la efectividad de los implantes de cápsulas esparcidas de radio en el tratamiento del carcinoma endométrico, aunque este efecto no es tan grande con la técnica multicapsular como con la del tratamiento en tándem. En otras palabras, la técnica multicapsular tiende a aminorar las desventajas impuestas por dichas irregularidades uterinas a la curieterapia intrauterina, de modo que hay más posibilidades de obtener con la misma un resultado efectivo. Los resultados descritos con esta técnica por Heyman y otros indican su superioridad desde el punto de vista clínico.

Radiation Therapy of Malignant Tumors of the Testis

Long-Range Statistical Analysis with a Review of the Literature[1]

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HISTORICAL SURVEY

THE LITERATURE contains numerous single case reports of malignant tumors of the testis but comparatively few studies of large series of cases. This is undoubtedly due to the comparative rarity of the disease. Cade (6) states that neoplasms of the testis comprise 1 to 1.5 per cent of all malignant tumors and 3 per cent of the malignant tumors of the genito-urinary tract in males. These figures compare favorably with those of Dean (12) of Memorial Hospital (New York), who found the respective incidences to be 2.09 and 3.39 per cent, whereas if all malignant tumors of both sexes were taken into consideration, the incidence amounted to 1.008 per cent. Chamberlin and Jamison (7), from the University of Pennsylvania, likewise noted an incidence of 1 per cent. Tanner (41), in an earlier publication, reported one case in every 2,000 hospital admissions, while Murray and Ewert (31) state that malignant tumors of the testis comprise only 0.5 to 0.6 per cent of all malignant neoplasms. In Army population, for obvious reasons, the incidence assumes a much higher value. Thus, Barner (1) observed that 7.2 per cent of all malignant neoplasms occurring in the white male personnel in 1941 were tumors of the testis.

The collective study of larger groups of cases dates back to the turn of the century. Kober in 1899 reviewed 114 cases and Chevassu (8) in 1906 published an excellent monograph dealing with about 100 cases. Tanner (41) in 1922 presented a series of 465 cases collected from the literature and 101 cases observed mostly at the Mayo Clinic. These initial reports were concerned mainly with the histologic features of the tumors and the results following simple orchiectomy. Desjardins, Squire, and Morton (13) in 1929 studied 101 cases; Rea (38) in 1931, 76 cases; Peirson (34) in 1932, 45 cases; Herger and Thibaudeau (21) in 1934, 63 cases from Buffalo; Desjardins, Counseller and Gianturco (14) in 1935, 155 cases; Hinman (24) in 1935, 54 cases; Smith, Dresser, and Mintz (40) in 1935, 100 cases collected from various Boston Hospitals; and Dean (12) in 1935, 292 cases from the Memorial Hospital in New York. Most of these reports dealt with the results of the radical operation of Chevassu and Hinman, the value of roentgen therapy, or the histologic features of the tumor. During the last decade additional valuable articles were published by Leddy and Desjardins (30) in 1938, 188 cases; Higgins and Buchert (22) in 1939, 81 cases; Cabot and Berkson (5) in 1939, 142 cases; Nash and Leddy (32) in 1943, 103 cases of seminoma; Barringer (3) in 1944, 69 cases; Scheetz and Leddy (39) in 1946, 32 cases of malignant teratoma; Friedman and Moore (19) in 1946, 922 cases; Kelby and Stenstrom (29) in 1947, 83 cases; and by others. Practically all of these later publications stress the great value of radiation therapy in the treatment of malignant tumors of the testis.

MATERIAL

To aid in the long-range statistical analysis, it was thought worth while to add to the above groups a series of 110 cases observed at Harper Hospital, Detroit, from 1923 to 1947.

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[1] From the Department of Radiology, Harper Hospital, Detroit 1, Mich. Presented at the Thirty-third Annual Meeting of the Radiological Society of North America, Boston, Mass., Nov. 30–Dec. 5, 1947.

In the statistical compilation of the results and the various factors relating to these results all cases were included whether the originally contemplated treatment was brought to a successful conclusion or remained incomplete. Likewise, patients who could not be traced were considered as dead from the time of the last known follow-up. In the entire series 2 cases were lost in the first two years, 2 were lost between two and five years, 4 between five and ten years, and 5 between ten and fifteen years. The majority of the lost cases disappeared during the time of the last war, when there was an unprecedented change of addresses, particularly in the Detroit area. Ten of the patients received only palliative treatment and in 3 of these orchiectomy was not performed. All deaths due to causes seemingly unrelated to the tumor are regarded as due to the malignant neoplasm in the recorded results.

TREATMENT

Treatment consisted, in the vast majority of the cases, of simple orchiectomy followed by extensive irradiation. Only if there was evidence of generalized metastases was the operation omitted. There are at least three reasons why a preliminary orchiectomy is indicated. First, there is considerable variation in the radiosensitivity of the cellular elements composing most primary malignant tumors of the testis, preventing their complete destruction by irradiation alone; second, the technical requirements for a uniform cross-firing of the testis are so difficult that it is practically impossible to meet them; and third, even with the best of protection, an injury to the normal testis cannot be avoided.

Irradiation was started within a few days after the operation. Because of the known tendency of the testicular tumors to early and widespread dissemination, attention was paid to the areas of regional invasion, as well as to those of probable distant extension, regardless of whether or not metastases had already taken place. Large sections of the body were exposed, numerous portals being used for the purpose of cross-firing. In the first series these included, as a rule, four to five portals for the pelvis and groins, three to four portals for the abdomen, centering on the para-aortic lymph nodes, four portals for the lungs and mediastinum, two portals for the supraclavicular and cervical lymph nodes, and in certain extremely malignant tumors, as for example chorionepithelioma, two portals for the skull. In the second and third series, which were given at intervals of eight to ten weeks, only the pelvis and abdomen were irradiated. The factors used were: 200 kv., 1 mm. Cu, 1 mm. Al; h.v.l. 1.9 mm. Cu; 50 cm. skin-target distance, and 15–20 r/min. intensity. In heavy patients, when a greater penetration was required, supervoltage roentgen therapy was employed. The factors here were: 500–600 kv., 60 cm. skin-target distance, and 20 r/min. Large portals were preferred, full doses being delivered in a single seance per portal, at the rate of one portal per day. The full dose amounted to 100 per cent SUD for the first, 90 per cent SUD for the second and 80 per cent SUD for the third series. For 200 kv., 1 mm. Cu, 100 per cent SUD represented 525 r in air (785 r with back-scatter); and for 500 kv., 7 mm. Cu, 675 r in air (925 r with back-scatter). The tumor or focal dose varied between 110 per cent SUD for the first and 70 per cent SUD for the third series.

In the statistical analysis, the long-range effect of the treatment just outlined was studied in relationship to the age of the patient; trauma, pain, and duration of symptoms prior to treatment; certain clinical features, as cryptorchidism, abnormalities of testis and gynecomastia; presence or absence of metastases; and the final results.

STATISTICAL ANALYSIS

Age of Patient: The oldest of our patients was seventy-two years of age and the youngest seventeen months. Tanner (41) stated that the vast majority of tumors of the testis occur during the years of greatest sex activity. This has been borne out by

TABLE I: MALIGNANT TUMORS OF THE TESTIS—AGE DISTRIBUTION

Age (in years)	Cases
0–9	4 (4%)
10–19	3 (3%)
20–24	10 (9%)
25–29	25 (23%)
30–34	19 (17%)
35–39	16 (15%)
40–44	15 (14%)
45–49	10 (9%)
50–59	6 (6%)
60 and over	2 (2%)

the observations of practically all investigators. Thus, Bailey (2) found the greatest number of his patients to be between thirty and forty years of age, Higgins and Buchert (22) between twenty and fifty years. Chamberlin and Jamison (7) reported 32 out of 45 as between twenty and forty years, and Smith, Dresser and Mintz (40) reported 58 per cent between twenty and forty years. More recently, Friedman and Moore (19), reviewing the data derived from study of 922 tumors of the testis collected at the Army Institute of Pathology between October 1940, when selective service began, and May 1946, found that seminomas and teratocarcinomas (comprising 70 per cent of tumors of the testis by their classification) appeared primarily between the ages of twenty and thirty-five. In our series, 71 per cent of the patients were between twenty-five and forty-five years of age, the average for the group being 33.5 years (Table I). This figure approximates that of Cabot and Berkson (5), who in 363 cases found the average age to be 36.2 years.

It is generally agreed that the adult type of carcinoma or malignant teratoma occurs more frequently in younger people and carries a poorer prognosis, whereas the seminomas or embryonal carcinomas are observed at a slightly later age and carry a better prognosis. Friedman and Moore (19) plotted the frequency distribution in relation to age in the form of a curve. The curve reached its peak at the age of twenty-three years for the teratocarcinomas and at thirty years for the seminomas. The immediate prognosis was bad for teratocarcinomas and good for seminomas.

In our series the relationship of age was studied in regard to the incidence of metastases at the time of institution of treatment and as it concerns the late results (Table II). To obtain a better evaluation of the particular age groups, all the cases treated were included in arranging the table. For example, of the total of 110 cases of the series, 35 belonged to the age group thirty to thirty-nine years, 43 per cent already having metastases at the time of the beginning of the treatment. In this age group, 34 out of the 35 cases received treatment two years or longer prior to the tabulation of the results, with a survival rate of 71 per cent; 30 out of the 35 cases received treatment five years or longer previously, with a 66 per cent survival rate; 21 out of the 35 cases ten years or longer previously with a 62 per cent survival rate, and 14 out of the 35 cases fifteen years previously with a 58 per cent survival rate. By so proceeding, it was found that this group between the ages of thirty and thirty-nine years had the highest survival rate for all periods

TABLE II: MALIGNANT TUMORS OF THE TESTIS—RELATION OF AGE OF PATIENT TO END-RESULTS

Age (in years)	No. Cases	Incidence of Metastasis	All Cases Treated Longer Ago Than							
			2 Years		5 Years		10 Years		15 Years	
			Cases	Survival	Cases	Survival	Cases	Survival	Cases	Survival
0–9	4	75%	4	25%	4	25%	3	33%	2	0
10–19	3	33%	3	66%	1	100%	..	..	..	..
20–29	35	43%	26	58%	23	56%	13	38%	5	0
30–39	35	43%	34	71%	30	66%	21	62%	14	58%
40–59	31	35%	23	61%	21	52%	16	25%	8	25%
60 and over	2	100%	2	0	2	0	1	0	1	0
TOTAL	110	43%	92	61%	81	55%	54	43%	30	33%

TABLE III: MALIGNANT TUMORS OF THE TESTIS—INCIDENCE OF TRAUMA AND PAIN

Trauma	
Present	30 cases (27%)
Absent	75 cases (68%)
Unknown or doubtful	5 cases (4%)
Pain	
Present	46 cases (42%)
Absent	59 cases (54%)
Unknown or doubtful	5 cases (4%)

studied. Although the frequency of metastasis originally was as great as in some of the other groups, the results remained throughout the most satisfactory. In the age group between forty and fifty-nine years the corresponding survival rate amounted to 61 per cent for the two-year, 52 per cent for the five-year, 25 per cent for the ten-year, and again 25 per cent for the fifteen-year period. In the group between twenty and twenty-nine years there was a more rapid decline, from 56 per cent at the five-year to 38 per cent at the ten-year and none at the fifteen-year period. In the very young the results were the worst.

Trauma: The significance of trauma in the causation and prognosis of malignant tumors of the testis has been debated by many observers. The following figures as to its frequency are given by various authors: Tanner (41), 22 per cent; Chamberlin and Jamison (7), 11 per cent; Smith, Dresser and Mintz (40), 13 per cent; Rea (38), 38 per cent; Nash and Leddy (32), 20 per cent; Kelby and Stenstrom (29), 15 per cent. Although these figures represent higher values than one could attribute to chance, several of the investigators are of the opinion that the role of trauma is negligible. Our series showed a positive history of trauma in 27 per cent of the cases (Table III).

To gain a better insight into the relationship between trauma and effect, a long-range study was carried out in our series by co-ordinating the incidence of trauma with the late survival rates. The results so obtained were tabularly arranged (Table IV) in a manner similar to that applied for an analysis of the influence of age, as shown in Table II. Two facts became apparent: first, the incidence of metastases at the time the patient reported for treatment was significantly higher in those cases in which trauma was absent; secondly, the cases with a history of trauma had a more favorable survival rate in all periods studied. This means that the history of trauma is significant in calling the patient's attention to the involved testis even if not directly responsible for the causation of the malignant neoplasm. Because of the earlier discovery of the lesion, treatment is started somewhat sooner, leading to a definite improvement of the final results.

TABLE IV: MALIGNANT TUMORS OF THE TESTIS—RELATIONSHIP OF PAIN AND TRAUMA TO END-RESULTS

	No. Cases	Incidence of Metastasis	All Cases Treated Longer Ago Than							
			2 Years		5 Years		10 Years		15 Years	
			Cases	Survival	Cases	Survival	Cases	Survival	Cases	Survival
Pain										
Present	46	44%	37	48%	33	48%	21	28%	7	0
Absent	59	41%	53	70%	45	62%	31	51%	22	46%
TOTAL	105	43%	90	61%	78	56%	52	42%	29	34%
Trauma										
Present	30	27%	23	63%	18	61%	14	43%	5	40%
Absent	75	48%	67	60%	60	55%	38	42%	24	33%
TOTAL	105	43%	90	61%	78	56%	52	42%	29	34%

Pain: The role of pain in the evaluation of the prognosis of the testicular tumors presents a rather interesting aspect. Tanner (41) reported the presence of pain in 52 per cent of 100 collected cases, but Dean (12) noted pain as part of the initial symptom complex in only 13 per cent of the cases seen at Memorial Hospital. In our series

TABLE V: MALIGNANT TUMORS OF THE TESTIS—RELATIONSHIP OF DURATION OF SYMPTOMS TO END-RESULTS

Duration of Symptoms (in months)	Cases	Incidence of Metastasis	All Cases Treated Longer Ago Than							
			2 Years		5 Years		10 Years		15 Years	
			Cases	Survival	Cases	Survival	Cases	Survival	Cases	Survival
0- 3	41	29%	34	71%	31	71%	15	60%	7	70%
4- 6	36	42%	28	50%	23	48%	19	31%	12	17%
7-11	11	55%	10	60%	8	50%	6	50%	4	50%
12 and over	22	64%	20	60%	19	42%	14	36%	7	12%
TOTAL	110	43%	92	61%	81	55%	54	43%	30	33%

the involved testis was painful in 42 per cent of the cases, whereas in 54 per cent there was no pain, and in 4 per cent the pain was doubtful (Table III). The long-range studies showed that when pain was present there was a slightly higher incidence of metastases at the start of the treatment and the survival rate was much poorer than when the swelling of the testicle was painless (Table IV). It is perhaps not too speculative to deduct from these observations that the pain in testicular tumors may be attributed to the rather rapid growth of the neoplasm, signifying a relatively poorer ultimate prognosis.

Duration of Symptoms: The duration of symptoms was regarded as the interval between the onset of definite, rapidly progressing symptoms and the time when the patient was first treated for the neoplasm. A number of patients gave a history of some abnormality of the testicle which outdated the onset of acute symptoms. The significance of these abnormalities will be discussed later. It was found that in 41 of our patients the symptoms lasted less than three months, in 36 between four and six months, in 11 between seven and eleven months, and in 22 twelve months or longer (Table V). There was a steady increase in the percentage of metastases found at the time the patient was first seen as the duration of symptoms increased. The figures of the survival rates were also very significant. The group at five years, with a duration of symptoms of less than three months, had a 71 per cent survival rate as compared with 55 per cent for the whole series or 42 per cent for the group in which the tumor was known to be present for twelve months or more. The intermediate groups showed some discrepancy, the five-year results being slightly lower when the onset of symptoms antedated the treatment by four to six months than when the interval was from seven to eleven months. This discrepancy may perhaps be attributed to the fact that the latter group was small, in which case a larger series of cases should correct the situation.

TABLE VI: MALIGNANT TUMORS OF THE TESTIS—LOCATION OF INVOLVED TESTIS

	Cases
Side	
Right	50 (45%)
Left	57 (52%)
Both	3 (3%)
Anatomical site	
Scrotal	98 (89%)
Inguinal	9 (8%)
Unknown	3 (3%)

To determine if throughout the years any progress has been made toward the goal of establishing an earlier diagnosis, we have also computed the average duration of symptoms during the first ten years and the last ten years of our series. It was found that from 1923 to 1932, inclusive, the average patient reported to his physician seven and one-third months after the onset of symptoms. From 1938 to 1947, inclusive, he waited for six and two-thirds months. Thus the net gain amounted to only twenty days per patient.

Clinical Features: In analyzing the influence of the various clinical features of testicular tumors on longevity, it was noted that the location of the tumor, cryptorchidism, other abnormalities of the testis, and gynecomastia had some effect. In 89 per cent of the cases in our series the

TABLE VII: MALIGNANT TUMORS OF THE TESTIS—RELATIONSHIP OF CLINICAL FEATURES TO DURATION OF LIFE AND 5-YEAR SURVIVAL

Clinical Features	Metastasis Present		Average Duration of Life in Fatal Cases		Alive Five Years	
	Cases	Per Cent	Cases	Months	Cases	Per Cent
Cryptorchidism	1	14	2	14	5	71
Other abnormalities of testis	4	40	3	18	10	70
Gynecomastia	1	14	2	14	5	71
Metastasis present			26	16	10	29
Metastasis absent			10	28	35	78

neoplasm arose from a testis occupying its normal position in the scrotum. In 8 per cent the involved testis was located in the inguinal canal, and in the remainder the location was not stated (Table VI). The right testis was the site of the lesion in 46 per cent and the left testis in 54 per cent of the cases. In 3 instances the involvement was bilateral.

Peirson (34), in 1932, collected from the literature 46 cases of bilateral tumors of the testis, to which he added a personal case of simultaneous involvement of both testes by a seminoma. Leddy and Desjardins (30) reported 4 instances in a series of 314 cases, whereas Smith, Dresser, and Mintz (40) found an incidence as high as 3 per cent in their cases. In none of our cases were both testicles involved at the same time. In one case there was an interval of nine years between the first tumor found, in the right testis, and the tumor of the left testis. The patient was well seven years following the second orchiectomy and deep roentgen therapy. In the second case there was an interval of four years between the two tumors. The patient is living and well fifteen years after his second operation followed by irradiation. Neither of these cases had clinical evidence of metastasis at any time.

The significance of cryptorchidism in the development of tumor of the testis is well substantiated, but the incidence is not agreed upon. Our incidence of only 7 per cent is lower than that of most observers. Other figures reported are: Nash and Leddy (32), 8.7 per cent; Chevassu (8), 11.7 per cent; Hinman (26), 12.2 per cent; Dean (12), 14.28 per cent; Higgins and Buchert (22), 8.4 per cent; Smith, Dresser, and Mintz (40), 5 per cent; Kelby and Stenstrom (29), 8 per cent. Murray and Ewert (31) of the Lahey Clinic found the incidence of malignant tumors in 694 cases of undescended testis to be 11 per cent, a ratio 48 times greater than in the normal. These authors stated that 97.5 per cent of developing tumors were on the ectopic side if one testis was descended. In an earlier report, Rea (38) concluded that an ectopic testicle had 220 times more chance of malignant change than a normal one, whereas Hinman and Benteen (27) thought that the chances were only 20 times as great. Gilbert (20) collected 841 cases of malignant tumors occurring in ectopic testes and noted that the incidence of neoplasm in the second testis was almost 1 in 4 if bilateral cryptorchidism was present. The above figures have been used as an argument for surgical fixation of the testicle lying in the inguinal canal to the scrotum, but Gilbert (20), reviewing 5,500 cases of surgically fixed testicles, found that, even so, neoplastic transformation ensued in 63 cases. According to Tanner (41), an ectopic testis lying in the abdomen undergoes malignant change only in very rare instances. A study of the survival rate in our few cases of malignant tumors based on cryptorchidism revealed that 71 per cent of the patients treated lived five years or longer (Table VII). This indicates that cryptorchidism was not an unfavorable clinical finding.

Fourteen cases in our series gave a history of some other abnormality of the testis prior to the development of tumor. These abnormalities included hydrocele, varicocele, hernia into the scrotum, and epididymitis. Similar observations were made by

TABLE VIII: MALIGNANT TUMORS OF THE TESTIS—LOCATION OF METASTASIS

Area Involved	At First Examination			Noted Secondarily	Noted Later
	Cases	Per Cent of All Cases	Per Cent of Cases with Metastases		
Abdominal lymph nodes	18	16	38	5	3
Inguinal lymph nodes	10	9	19	5	..
Generalized metastasis	8	7	16	..	7
Extension along spermatic cord	7	6	15	1	..
Lungs	7	6	15	8	1
Left supraclavicular nodes	4	4	8	1	..
Deep pelvic nodes	4	4	8	1	..
Mediastinal nodes	2	2	4	..	..

a number of investigators. Dean (12), for example, found a history of hernia in 12 per cent of his cases, Nash and Leddy (32) noted hydrocele in 19.4 per cent of seminomas, Scheetz and Leddy (39) reported hydrocele in 13 per cent and varicocele in 4 per cent of malignant teratomas, and Kelby and Stenstrom (29) described hydrocele in 6 per cent of their cases. It thus appears that tumors of the testis occur more frequently in patients with histories or findings of various abnormalities than in the normal. A study of the survival rate here, too, showed that 70 per cent of the patients were well at the end of five years (Table VII).

Gynecomastia was observed in 7 cases of our series. This figure compares favorably with those of Smith, Dresser, and Mintz (40), 5 per cent; of Chamberlin and Jamison (7), 11 per cent; Scheetz and Leddy (39) 10 per cent; and others. In some of the cases reported there was marked hypertrophy of the breast accompanied by a secretion from the nipple. In one of our cases, eighteen months following orchiectomy and one year after roentgen therapy, pain and swelling developed in the left breast. This was treated by irradiation and became symptomless within three weeks only to be followed by pain and a diffuse infiltration of the subareolar tissue of the right breast, with an area of hard induration the size of a quarter. This was treated in the same manner and cleared up similarly. One month later the patient had a ruptured appendix, entered the hospital as an emergency case, and finally expired of generalized peritonitis. Postmortem examination revealed no evidence of the malignant tumor. In the group with gynecomastia the five-year survival rate was again 71 per cent (Table VII).

The comparatively greater proportion of favorable results in the cases exhibiting the clinical complications of cryptorchidism, testicular abnormalities, and gynecomastia is attributed, as in the case of trauma, to the fact that the patient's attention is drawn to his ailment sooner, thereby permitting institution of the treatment at a somewhat earlier stage of the tumor.

Metastases: In 43 per cent of our cases metastases were clinically evident when the patient first reported for treatment. The figures collected from the literature show, under similar circumstances, a variation between 40 and 72 per cent. In those cases of our series in which death occurred within the first five years there was an average duration of life of sixteen months in the group with initial metastases and of twenty-eight months in the group without evidence of metastases (Table VII).

Desjardins (15), in 1939, called attention to the fact that malignant neoplasms of the testis spread first to the para-aortic lymph nodes above the entrance of the spermatic vessels, then to the "sentinel" left supraclavicular nodes, and only later to the lungs and other parts of the body. Our group with initial metastases showed extension to the para-aortic lymph nodes in 38 per cent, to the left supraclavicular lymph nodes in 8 per cent, and to the lungs in 15 per cent of the cases. In addition

TABLE IX: MALIGNANT TUMORS OF THE TESTIS—PROGNOSTIC VALUE OF THE 2-YEAR SURVIVAL

	2-Year Results		5-Year Results	
	Cases	Alive	Cases	Alive
With metastasis	36	11 (31%)	36	10 (29%)
Without metastasis	45	41 (91%)	45	35 (78%)
TOTAL	81	52 (64%)	81	45 (55%)

there were 16 per cent having generalized metastases (Table VIII). Nash and Leddy (32) found that 24.2 per cent of their cases had metastases to the paraaortic lymph nodes and only 2 per cent to the lungs. Smith, Dresser, and Mintz (40) earlier reported a 34 per cent involvement of the "lumbar glands," and 23 per cent involvement of the lungs.

The distribution of metastases in all cases of our series, whether they were observed initially or occurred after treatment was begun, is shown in Table VIII. One interesting feature of these figures is that the inguinal lymph nodes were involved in only 19 per cent of the cases with initial metastases. Leddy and Desjardins (30) pointed out that extension to the groin does not develop unless the malignant neoplasm has broken through the capsule of the testis. Barringer (3), of the Memorial Hospital, believes that in some cases the extension to the groin is the result of the surgeon cutting into the tumor at the time of operation and implanting tumor cells into the wound. He reported the following incidence of metastasis to various lymph node areas in 37 cases of malignant tumors of the testis brought to autopsy: celiac 56.9 per cent, lumbar 54.6 per cent, mediastinal 48.7 per cent, pelvic and iliac 37.9 per cent, cervical 35.2 per cent, bronchial 35.2 per cent, mesenteric 18.9 per cent, and inguinal 10.8 per cent. In other words, during the natural sequence of events, the inguinal lymph nodes were involved less frequently than any other lymph node group of the body. Barringer also found that extension along the spermatic cord was a bad diagnostic sign. We observed such an extension in 7 of our cases presenting themselves for treatment, and only 1 of them survived the five-year period.

TABLE X: MALIGNANT TUMORS OF THE TESTIS—RELATIONSHIP OF METASTASIS (BEFORE TREATMENT) TO END-RESULTS

	All Cases Treated Longer Ago Than								Total Cases
	2 Years		5 Years		10 Years		15 Years		
	Cases	Survival	Cases	Survival	Cases	Survival	Cases	Survival	
With metastasis	39	31%	36	29%	27	19%	14	7%	47
Without metastasis	53	85%	45	78%	27	66%	16	50%	63
TOTAL	92	61%	81	55%	54	43%	30	33%	110

Results: The rate of survivals was analyzed for the two-, five-, ten-, and fifteen year periods. The two-year period was included to determine if a shorter period of observation might not give sufficient information as to the final outcome of the case. As already mentioned, the average life duration in those cases where death occurred during the first five years was sixteen months from time of the first symptom in the group with initial metastases. This made it probable that there may be only a slight difference between the two-year and five-year survival figures and that if a patient passed the two-year period without the appearance of metastases the chances for a final cure may be quite good. A compilation of the two-year and five-year survivals is shown in Table IX. As may be noted, for the group with initial metastases the two-year survival amounted to 31 per cent and the five-year survival to 29 per cent.

TABLE XI: MALIGNANT TUMORS OF THE TESTIS—RESULTS WHERE ONLY ORCHIECTOMY WAS DONE

Authors	Cases	Results—Per Cent Survival		
		3 Years	4 Years	5 Years
Kober (1899)	53	18	..	..
Chevassu (1906)	100	..	19	..
Tanner (1922) (Lit.)	425	..	5.3	..
Tanner (1922) (Pers.)	79	..	22	..
Rea (1931) (Lit.)	257	..	13.2	..
Rea (1931) (Pers.)	34	..	13.2	..
Hinman (1933) (Lit.)	258	..	..	5.6
Hinman (1933) (Radical)	100	..	..	17
Higgins and Buchert (1939)	32	..	..	24

In the cases without evidence of metastases at the time treatment was started, the respective figures were 91 and 78 per cent. It thus would seem that the two-year survival rate would constitute a good prognostic index in about 90 to 95 per cent of the cases.

The survival rates for all periods up to fifteen years are shown in Table X. In the group with initial metastases, the survivals were 29 per cent at the five-year, 19 per cent at the ten-year, and 7 per cent at the fifteen-year period. These results were rather surprising. They furnish undoubted proof that malignant neoplasms of the testis should not be considered hopeless from the point of view of advisability of radiation therapy, even when there is evidence of regional or more distant metastases. In fact, the figures obtained constitute higher values than in some of the operable groups reported in the literature in which, since there was no evidence of metastases at the time of the operation, radiation therapy was omitted as part of the treatment. The group without evidence of initial metastases in our series gave a survival of 78 per cent at the five-year, 66 per cent at the ten-year, and 50 per cent at the fifteen-year period. If all cases are counted together, the survivals were 55 per cent at the five-year, 43 per cent at the ten-year, and 33 per cent at the fifteen-year period.

To obtain a still better evaluation of the merit of radiation therapy, the available statistics were collected from the literature for those instances in which surgery alone was used and those in which a combination of surgery and radiation therapy was employed. Table XI shows the three-, four-, and five-year results obtained by various authors between 1899 and 1939 when only orchiectomy was done. The highest percentage of five-year survivals was 24. Table XII is a compilation of the results published by various authors between 1933 and 1947 for two-, three- and five-year periods when a combination of orchiectomy and extensive radiation therapy was used. The lowest percentage of five-year survivals was 25 per cent for malignant teratoma and the highest 67.7 per cent for seminoma. If no pathologic distinction was made between the neoplasms, the average five-year figure

TABLE XII: MALIGNANT TUMORS OF THE TESTIS—RESULTS WITH ORCHIECTOMY AND RADIATION THERAPY

Authors	Cases	Results—Per Cent Survival		
		2 Years	3 Years	5 Years
Desjardins, Counseller, and Gianturco (1933)	125	..	..	48
Leddy and Desjardins (1938)	72	..	59.7	53.1
Cabot and Berkson (1939)	110	..	61	52.4
Higgins and Buchert (1939)	41	..	..	35.5
Nash and Leddy (1943) (seminoma only)	103	..	..	67.7
Barringer (1944)	69	..	..	59
Scheetz and Leddy (1946) (malignant teratoma)	32	..	34.4	25
Kelby and Stenstrom (1947)	83	48	..	29
Leucutia, Evans, and Cook (1947)	110	61	..	55

amounted to about 50 per cent or slightly better.

SUMMARY AND CONCLUSIONS

1. One hundred and ten cases of malignant tumor of the testis are reported and analyzed from the point of view of results up to fifteen years. In compiling the statistics all cases are included whether treatment was satisfactorily completed or not, so that the figures obtained constitute absolute values.

2. The age of the patient, the history of pain and trauma, and the duration of symptoms are considered in their relationship to end-results and incidence of metastases at the time treatment was started. It was found that patients in the fourth decade of life have the best prognosis, that history of pain is an unfavorable finding, and that the patients with a history of trauma have a better average chance for survival. When the symptoms, prior to treatment are of short duration fewer metastases are observed at the time of initial examination and the long-range survival rate is more favorable.

3. The clinical findings of cryptorchidism, other abnormalities of the testis, and gynecomastia do not influence the prognosis unfavorably since the patient's attention is likely to be called to his ailment sooner than when these complications are not present.

4. The presence of metastases at the time of institution of treatment does not mean that the patient has no chance for a long survival. In 43 per cent of the cases in the series there was clinical evidence of metastases when the patient first reported for treatment. In this group the survivals were 29 per cent at the five-year, 19 per cent at the ten-year, and 7 per cent at the fifteen-year period.

5. The best treatment for malignant neoplasms of the testis is simple orchiectomy followed by extensive roentgen therapy. A comparative analysis of the results in which surgery alone and surgery combined with irradiation were used shows a very marked superiority of the latter. The over-all survivals for the series amounted to 55 per cent at the five-year, 43 per cent at the ten-year, and 33 per cent at the fifteen-year period.

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SUMARIO

Radioterapia de los Tumores Malignos del Testículo

1. Al comunicar 110 casos de tumores malignos del testículo, se les analiza con respecto a los resultados hasta a los 15 años. Al compilar las estadísticas, se agregaron todos los casos, ya se hubiera o no completado satisfactoriamente el tratamiento, de modo que las cifras representan valores absolutos.

2. La edad del enfermo, la historia de dolor y traumatismo y la duración de los síntomas son consideradas en su relación con los resultados terminales y la incidencia de metástasis al iniciarse el tratamiento. Descubrióse que los enfermos en el cuarto decenio de sus vidas muestran el mejor pronóstico, que la historia de dolor es un hallazgo desfavorable y que los enfermos con antecedentes de traumatismo tienen por término medio más probabilidades de sobrevivencia. Cuando los síntomas, antes del tratamiento, han durado poco tiempo, obsérvanse menos metástasis al hacer el examen inicial y la tasa de sobrevivencias de largo plazo es mayor que cuando el enfermo deja pasar tiempo sin consultar al médico.

3. Los hallazgos clínicos de criptorquidia, de otras anomalías del testículo y de ginecomastia no afectan el pronóstico desfavorablemente, dado que pueden hacer que el enfermo se fije en su dolencia antes de lo que haría si no existiesen tales complicaciones.

4. La presencia de metástasis al iniciarse el tratamiento no denota que el enfermo no tenga probabilidades de una sobrevivencia larga. En 43 por ciento de los casos de la serie había signos clínicos de metástasis al presentarse el sujeto por primera vez para tratamiento. En este grupo las sobrevivencias sumaron 29 al cumplirse los cinco años, 19 por ciento a los diez años y 7 por ciento a los quince años.

5. El mejor tratamiento de las neoplasias malignas del testículo es la orquiectomía simple seguida de la roentgenoterapia extensa. Un análisis comparado de los resultados obtenidos con la cirugía sola y la cirugía combinada con la irradiación revela la superioridad muy pronunciada de la última. La sobrevivencia global para la serie ascendió a 55 por ciento a los cinco años, 43 por ciento a los diez años y 33 por ciento a los quince años.

Treatment of Deep-Seated Malignant Tumors With Multiple-Port Technic Simulating Rotation Therapy[1]

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THE TREATMENT of deep-seated tumors, particularly of the esophagus and of the lung, has been primarily surgical, since until recent times, irradiation has not proved successful. The difficult problem that radiation therapy has had to meet, in order to eradicate successfully such deep-seated neoplasms, is the necessity of delivering to the tumor a destructive dose without adverse effect upon the skin and overlying tissues. The successful solution of this problem has been sought for many years, with but slight success. It seems logical to assume, however, that clinically, as well as pathologically, a number of deep-seated carcinomas are essentially amenable to external radiation therapy, and that an improvement in technical details may insure curability of a certain percentage of these, as is true of carcinomas located in more accessible positions.

That the factor of inaccessibility is at least in part responsible for the failures of radiotherapy in these deep-lying lesions is suggested by the observation that accessible but pathologically similar tumors of the oral cavity, hypopharynx, and cervix uteri can be controlled in a very much higher percentage of cases by irradiation. The poor results in carcinoma of the esophagus are all the more disappointing in view of the fact that it is a disease that remains localized until a comparatively late stage in its history and often does not present the factor that makes for failure in similar growths in other situations—namely, early involvement of the lymphatics. It is evident, therefore, that the obstacle to complete sterilization of deep-seated radioresponsive tumors may frequently be the inability to deliver an adequate tumor dose.

Stone (1) says that the aim of irradiation is to deliver to the tumor the most effective homogeneous dose produced by just enough energy to secure the desired result. Properly used, 200-kv. x-ray therapy can cure as many or nearly as many deep-seated cancers as higher voltages, but to achieve this result, great skill is required on the part of the radiologist and considerable endurance on the part of the patient. Holmes and Schulz (2) believe that supervoltage therapy offers some advantages, since it is less likely to produce serious skin damage. Stone also notes that the higher-voltage therapy more readily irradiates and is less likely to produce adverse reactions.

The problem, however, of delivering a destructive dose to a deep-seated tumor is not simply one of increased physical power. Although the voltage employed in irradiation is an important factor, merely increasing this does not insure an adequate or efficient tumorcidal dosage to deep-seated neoplasms.

Two types of cancer which have defied our efforts at effective control by irradiation are cancer of the esophagus and cancer of the lung. In these conditions supervoltage irradiation was at first thought to be the solution of the problem. Because the use of extremely high voltages permits the administration of large doses of radiation

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to deep-seated tumors with minimal effect upon superficial tissues, supervoltage therapy has been used at Memorial Hospital for the treatment of esophageal cancer, as reported by Watson (3). Whether or not, however, supervoltage irradiation, with its moderate effect on the superficial tissues, is more effective in cancer of the esophagus than the customary high-voltage x-rays is still conjectural. In a series of advanced esophageal cancers treated with supervoltage x-rays reported from Holland (4), none was cured. Neither were any cures obtained with this technic in cancer of the lung. Holmes and Schulz stated that no patient with carcinoma of the esophagus treated by them with supervoltage irradiation survived longer than two years. Of 5 patients treated by Buschke and Cantril (5), at 800 kv., 100 cm. distance, 1 was alive after three and a half years without radiologic evidence of recurrence. These authors believe that super voltage irradiation is well tolerated, with milder after effects; yet they consider 200-kv. radiation justifiable and prefer it to surgery. It produces uniformly palliative results, which they believe are quite worth while, and the patients usually remain in good condition six to eighteen months after treatment.

Unfortunately, however, the attitude regarding the control of deep-seated tumors by x-ray therapy is almost universally one of pessimism. Levitt (6), while reporting locally effective results, stated that most patients succumbed to pulmonary lesions attributable to the irradiation. Steele (7) stressed the gloomy outcome of both surgery and irradiation.

Harnett (8), studying the cases under the jurisdiction of the British Empire Cancer Campaign, noted that deep roentgen therapy prolonged life in cases of cancer of the esophagus to twelve months as compared to nine months without treatment. Smithers and his associates are more optimistic. They treated 54 patients, with partial or complete relief of symptoms in 39; 18 lived one year or longer. No instance of pulmonary fibrosis was noted in their series. The treatment factors used by these workers are: 400 kv., 80 cm. distance, 6 fields, 4 of 15 × 4 cm. and 2 of 15 × 6 cm. All 6 fields are treated daily, the dose per field per day being usually that which will give a tumor dose of 6,000–7,000 r in five to six weeks.

During the course of the past few years several methods have been suggested for delivering a homogeneous destructive tumor dose to deep-seated neoplasms. In 1937 Dessauer and his associates (10) suggested that effective irradiation could be accomplished by rotating a patient about a fixed focus of x-rays, designating this technic as the Istanbul rotation method. The main virtues of the method are greater depth dose with minimal surface irradiation, the tumor being constantly within the x-ray beam, whereas only that part of the skin which happens to be in the beam during the particular phase of rotation is irradiated. Greater doses, 9,000 to 10,000 r, can thus be administered with impunity.

Friedman and Lorenz (11) devised a method of applying a double beam of x-rays to opposite sides of the lesion to be treated. By simultaneous irradiation with two x-ray tubes through two opposite portals, they found it possible to approximately double the dose to the tumor without increasing the skin dose.

Nielsen (12) in 1945 reported on the treatment of esophageal cancer by rotation therapy, under fluoroscopic control. The patient is seated on a stool rotating about a vertical axis, while the roentgen tube is in a fixed position with the central ray directed horizontally. Nielsen believed, as a result of his clinical experience with 174 cases, that with this type of rotation therapy, particularly in cancer of the intrathoracic portion of the esophagus, better results may be obtained than with any method previously used.

More recently Munson (13) has devised a method of rotating the beam continuously about an axis passing through the lesion. This is said to afford greater immobilization of the patient and greater accuracy in obtaining theoretical distribution of the radiation.

In 1940 Leddy and Moersch (14) reported the use of massive doses of x-rays through multiple ports (four) and, in some cases, protracted therapy to multiple ports (four to six) to attain their object in treating deep-seated tumors. They administered 560 r per area by the former method and 200 r per treatment by the latter, for a total of 2,000 to 3,000 r per field.

On the basis of suggestions reviewed above, we devised the Bellevue method of rotation therapy through multiple fixed fields. The theory of this multiple-port method and its use in practice are based on the fact that the center toward which the beam is directed will be exposed to intense homogeneous treatment while each field of the skin surface, because of the rotation, will receive only a fraction of the total dose.

By means of physical calculation and measurements, we can demonstrate that it is possible to introduce adequate cancer-sterilizing doses into deep-seated tumors with 200-kv. radiation. The factor determining cure or failure will be the histology of the tumor, not the dose. Nielsen attempted with fair success to give an adequate tumor dose in cases of carcinoma of the esophagus. Strandqvist (15) found that those patients with carcinoma of the esophagus who remained well for two years after irradiation had received a tumor dose of 4,350 to 5,000 r over a period of thirty-five to forty days. He believed that, were it possible to apply a total tumor dose of 5,000 to 6,000 r in thirty to forty days, improved results would follow.

To get such favorable effects the Bellevue plan of rotation therapy through multiple fixed ports was developed. With this technic of multiple-port irradiation, a tumor dose which is probably adequate can well be applied to these deep-seated lesions. Even for palliation, a high total dosage is necessary. It is evident that esophageal carcinoma lends itself particularly well to rotation therapy, owing to the almost central location of the esophagus in the longitudinal axis of the thorax.

Though originally planned for carcinoma of the esophagus, the method has also been used for localized and solitary primary neoplasms of the lung parenchyma and hilar regions. The results in these cases are gratifying from the standpoint of relief of symptoms, prolongation of life, and shrinkage of the tumor.

The palliative effect following this method of treatment is marked. All the patients treated for cancer of the esophagus were able to swallow normally after an adequate tumor dose was administered. This in itself was most gratifying, considering the fact that in all the disease was in an advanced stage.

A disadvantage of rotation therapy via multiple ports is that a large volume of normal tissue must be irradiated, that damage may be done to this tissue, and that the tumor dose which can be administered is limited by the total energy absorption that the patient will tolerate.

This multiple-port technic, however, has much to recommend it, for it permits an even irradiation of the whole tumor. It is the most effective method of delivering a suitable depth dose and at the same time causing the least discomfort. Although it is true that a large volume of tissue is irradiated, each area receives only a relatively small amount of radiation, due to the fact that, with the great number of portals used, each one receives but a small number of treatments. The interval between treatments to any one portal is long enough to allow the overlying tissue to recuperate partially before it is treated again. In this way there is a maximum tumor effect with minimum damage to the overlying normal tissues. It is important, however, that very careful attention be given to obtaining the optimal distribution of the radiation by accurate arrangement of the fields and accurate application of the angles of the radiation beam. By such means it is hoped to deliver an adequate tumor dose without overstepping either the limit of total energy absorption that can be tolerated, or the dose which would cause serious damage to the normal tissues.

In treating thoracic neoplasms, it is not

always possible to avoid radiation pneumonitis or fibrosis. If a real attempt to control the malignant condition is made, radiation must be applied in such strength that it is bound to inflict some lung damage. A limited degree of pneumonitis produces little in the way of symptoms or permanent functional impairment, but in a certain percentage of cases severe radiation damage to a large portion of the lung and mediastinum will develop, with intolerable after-effects. However, this must be chanced when it is remembered that we are dealing with a disease that is otherwise practically 100 per cent fatal.

permit measuring the tumor distance from the skin over the sternum and thoracic spine.

In order to secure the requisite daily dose to the growth and yet not exceed the tolerance of the skin and underlying structures, twelve portals of entry are used for esophagus and hilar lung tumors. By taking advantage of so large a number of fields and planning treatment so that any particular skin field was not submitted to irradiation more than once a week, it was hoped that the danger to the underlying structures could be mitigated. With multiple narrow fields, the esophagus receives a

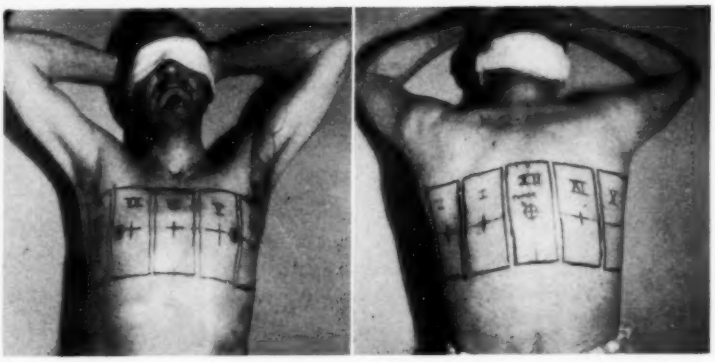


Fig. 1. Distribution of the portals for a mid-third esophageal carcinoma.

In order to carry out the multiple port plan of therapy, a special preparatory procedure is outlined. Because proper direction of the beam of x-rays is important, the exact extent and site of the tumor, wherever situated, must be precisely determined.

In the case of cancer of the esophagus, the extent and location of the tumor must be determined by means of a teleoroentgenogram taken in the true lateral and posteroanterior positions with a Bucky grid. A swallow of barium is given and fluoroscopy is done with the patient in a vertical position with arms extended cephalad. During fluoroscopy, indicators, one on the front and one on the back of the chest, are fixed directly over the center of the lesion and the extent of the tumor is determined in relation to these. The indicators also

much larger dose, while the parts of the lung distant from it receive no more than they did by older methods. The twelve portals are outlined on the front and back, and in the axillae, just as figures are placed on a clock (Fig. 1). Fewer ports are used for lung tumors eccentrically placed, since, for example, a tumor dose *via* a left axillary portal would contribute very little to a right-sided lesion.

While it is necessary to work with the narrowest possible fields in order to take full advantage of these multiple ports, care must be taken that the broad diameter of the field is wide enough to cover the whole breadth of the tumor, so that the latter is irradiated homogeneously. This can be insured, as a rule, by using a field 5 to 6 cm. wide. It was found, however, that the circumference of the average chest will accom-

modate twelve ports, each 7 cm. wide, with intervals of 1 cm. between ports and there would thus be less chance of misdirecting the incident beam to the underlying tumor.

The dimensions of the field in the long axis of the esophagus, on the other hand, were made much greater than was necessary to cover the growth, because of the well known tendency of the disease to spread up and down the esophagus. In addition, the increase in scattered rays obtained with a larger field enhances the depth dose. Fields 7 × 15 cm. were therefore used for the esophageal cancers. The length of the field in the lung cases depended on the size of the tumor.

With these narrow portals, the incident beam must be directed with the greatest possible accuracy to cross-fire exactly on the tumor. A deviation from the stated angle may cause an undesirable disturbance of the distribution of the intensity in the thorax, to the damage of the normal tissue at the expense of the tumor. In addition, the beam may entirely miss a small deep-seated tumor or, if the tumor is sufficiently large, may strike only its edge. A high degree of accuracy was secured by using the "Demy protractor" (16). This is a translucent protractor having a radius of 20 cm. and adjustable on two parallel measuring sticks, one on each end (Fig. 2).

To use this device, the patient is first placed on his back in the treatment position and twelve 7 × 15-cm. portals are marked out on the skin. The protractor is placed over the chest with the zero degree over the center of the field directly overlying the tumor. The protractor is elevated on the two parallel measuring rods to a position corresponding to the distance from the skin over the dorsal spine to the tumor. This distance, as previously stated, is determined by lateral teleoesophagrams. A measuring rod is placed in the center of each portal in rotation and parallel to the nearest angle of the protractor. The angle of the correct incident beam can be

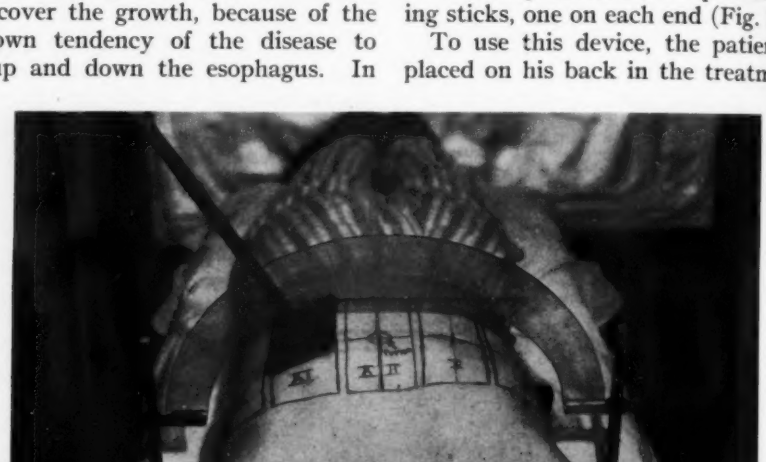


Fig. 2. Demy protractor in position for measuring angles and depth of tumor.

read off on the protractor and, in addition, the distance from the skin over the various portals to the tumor can be read on the measuring rod, which is calibrated equivalent to the radius of the protractor. The patient is then turned face down and the protractor elevated or depressed on the measuring rods to correspond to the distance from the skin over the sternum to the tumor and the same angling procedure is carried out over the posterior portals. In this way it is possible to determine not only the proper angles of the incident beam from each portal to the tumor, but also the tumor distance from each portal. The angulation of the field in relation to the esophagus is checked at each setting.

When the tumor is situated behind the clavicle, a different arrangement of fields is used, for at this level the projection of the shoulders makes the lateral fields useless, owing to their distance from the center. Five fields are placed on the front of the chest and five similar areas on the back, one central and two on either side. In addition, there are four fields, 5 × 5 cm., at the root of the neck; through these the beam is directed slightly downward. The surface dose here is much smaller than that given to growths lower down, but, on the other hand, upper growths are less deeply situated, the esophagus as it passes behind the manubrium sterni being only a few centimeters from the surface.

The amount of radiation required to eradicate completely a deep-seated tumor is still not definitely determined, but experience with tumors of s milar histology in other locations permits the assumption that approximately 5,500 to 6,500 r delivered to the tumor within four to five weeks may be the average sterilizing dose required for the treatment of esophageal cancer. Treatment in the cases to be described here was administered with the following factors: 200 kv., 20 ma., 50 cm. distance, Thoraeus filtration, h.v.l., 1.9 mm. Cu.

The preparation and care of the patient during treatment are of the utmost importance. Adequate nourishment and a high caloric intake must be maintained. Nutramigen and other high-calorie, high-protein, high-vitamin, well balanced liquid foods were given in our cases where the obstruction was almost complete and the patient could swallow only sips of fluid. When more solid food was tolerated, this was recommended, as it acted like a bougie and kept the esophagus from contracting if fibrous displacement occurred. Vitamin

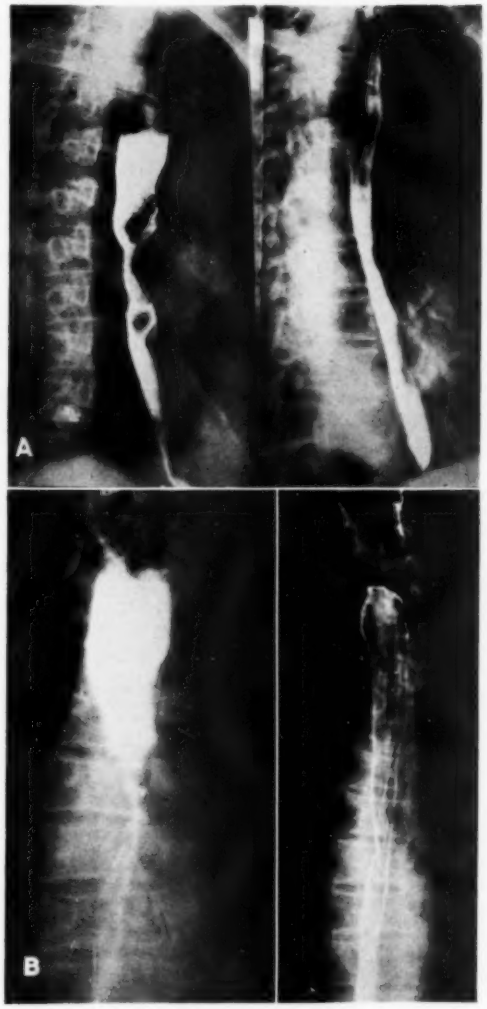


Fig. 3. Case I: Carcinoma of the middle third of the esophagus. A. Before treatment and two months after treatment, oblique view. B. Postero-anterior view before treatment and two months after treatment, showing re-establishment of longitudinal mucosal folds.

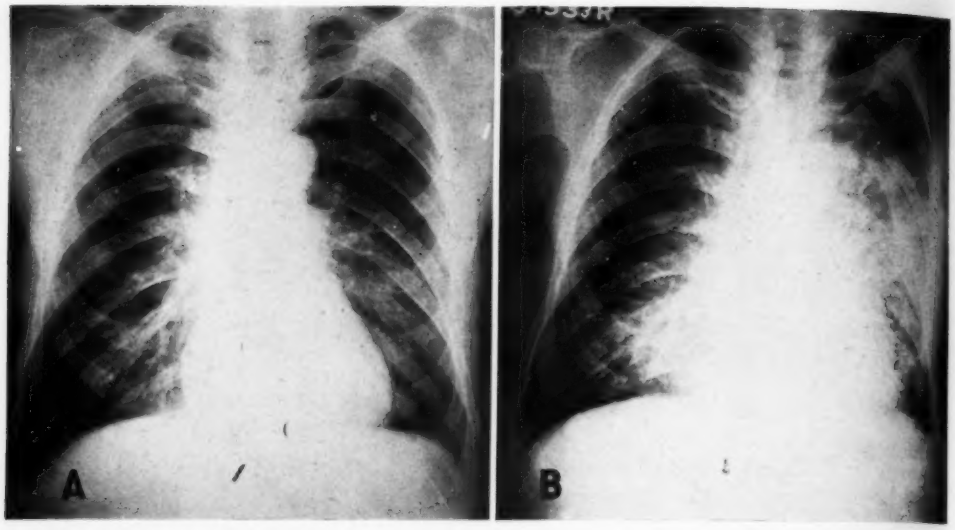


Fig. 4. Case I: A. Roentgenogram of lung before treatment. B. Roentgenogram of lung three and a half months after treatment, showing fibrosis of left mid-lung and right paracardiac area, with heart slightly drawn to left.

B_6 in the form of pyridoxine, 50 mg., one hour before and one hour after treatment, intramuscularly, was found to be extremely successful in preventing radiation sickness. Blood counts were carried out before treatment and at weekly intervals throughout its course, since it is here that the first indication of failing tolerance to large volume irradiation appears.

CARCINOMA OF THE ESOPHAGUS: CASE REPORTS

CASE I: A. J., 63 years old, white male, was admitted Dec. 19, 1946, because of difficulty in swallowing and a 15-pound weight loss in the preceding month. Esophagoscopy and a biopsy specimen taken from a friable hemorrhagic mass proved the condition to be a carcinoma. The esophagram showed evidence of extensive infiltration involving the upper and middle thirds of the esophagus. Exploratory thoracotomy revealed an inoperable carcinoma adherent to the hilar structures. X-ray examination of the chest was essentially negative.

Treatment: The patient received rotation x-ray therapy through 12 portals around the thorax (Fig. 1) from Feb. 24 to March 19, 1947. Two portals were treated daily in rotation. Each portal received 600 r (air) to a total of 1,800 r (air). The total skin dose per portal was 2,250 r and the tumor dose 5,800 r in 24 days elapsed time or 18 treatment days.

Course: On the sixth day of treatment there was a beginning esophagitis characterized by a substernal burning sensation during eating. The weight was 120 pounds and a beginning first degree epidermitis appeared. By the fifteenth day of treatment swallowing had improved. On the twenty-ninth day after the beginning of treatment, the patient was taking a full regular diet and his weight was 122 pounds. There was still some esophagitis. By the thirty-ninth day a superficial dry desquamation developed over the treated skin areas, which healed by the fifty-third day. On April 21, 1947, repeat esophagrams revealed no evidence of malignant infiltration of the esophagus (Fig. 3) and the weight was 126 pounds. At this time the patient began to cough, and roentgenograms of the lungs showed extensive pneumonitis involving the parahilar regions. On May 27, 1947, esophagoscopy showed a small ulceration. Report on a biopsy of its edge read: "No tumor tissue seen." The rest of the esophagus was smooth and somewhat narrowed. By May 31, 1947, three months after the beginning of treatment, dyspnea, chills, and low-grade fever developed. Fine and coarse râles were heard throughout both lung fields. The impression at that time was bronchopneumonia and radiation fibrosis (Fig. 4).

The patient died on June 19, 1947, about four months after the beginning of treatment. Postmortem examination revealed the following pertinent findings: in the esophagus, changes consistent with a chronic esophagitis and periesophagitis; no tumor cells; in the lungs, evidence of a chronic pneumonitis with organization, findings concomitant with a radiation pneumonitis.

Comment: This case proved that an esophageal tumor could be sterilized with

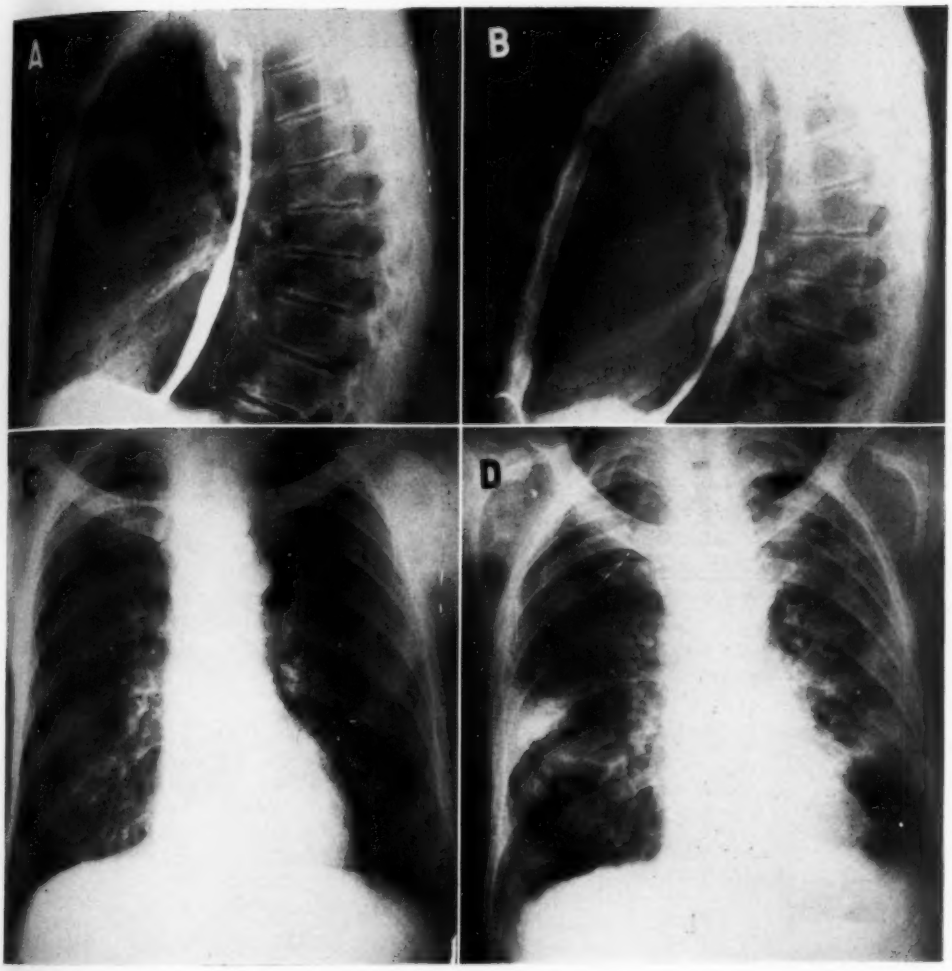


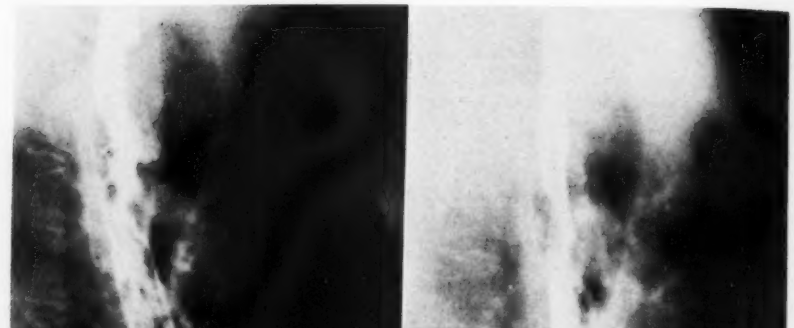
Fig. 5. Case II: Carcinoma of mid-third of esophagus. A. Before treatment. B. Two months after treatment. C. Roentgenogram of lungs before treatment. D. Roentgenogram of lungs three and a half months after beginning of treatment, showing bilateral pulmonary fibrosis and bronchopneumonia.

the doses used. It also showed that our technic would have to be modified in order to avoid lung damage.

CASE II: M. R., a 67-year-old white male, was admitted on May 15, 1947, complaining of difficulty in swallowing solid foods since July 1946 and a 30-pound weight loss. Three months earlier, at another hospital, esophagoscopy had revealed an irregular mass beyond the cricopharyngeal area, proved by biopsy to be squamous-cell carcinoma. Esophagrams revealed evidence of malignant infiltration of the esophagus at the junction of the upper and middle thirds. X-ray examination of the lungs was essentially negative. A Janeway gastrostomy and an exploratory thoracotomy done at the other hospital revealed an inoperable carcinoma of the esophagus. Biopsy of a cervical lymph node showed squamous-cell carcinoma.

Treatment: Between May 19 and June 10, 1947, the patient received through 12 fields a tumor dose of 6,170 r in 23 days elapsed time and 16 treatment days. Each port received 600 r (air) or 750 r (skin). Some of the portals were irradiated twice, some three times.

Course: Before the beginning of treatment, the patient could swallow nothing but liquids, and these spilled out of the gastrostomy opening. By the seventh day of treatment the weight was 115 pounds and small pieces of solid food could be swallowed.



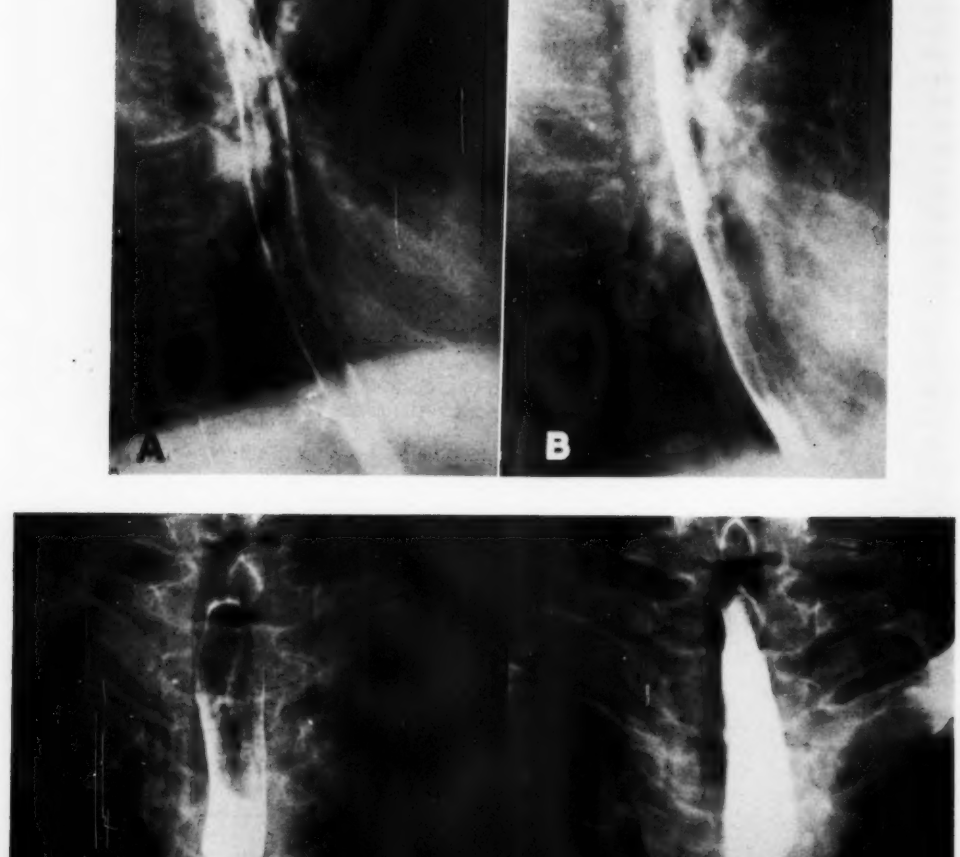


Fig. 6. Case III: Infiltrative carcinoma of the mid-third of esophagus. A. Before treatment. B. Five months after beginning of therapy, showing regression of the tumor. C. Postero-anterior view before treatment. D. Postero-anterior view of same case after treatment.

By the fourteenth day of treatment there was a gain of 2 pounds; the patient was eating well but losing most of the food through the gastrostomy opening. On the twenty-third day an esophagitis developed, characterized by pain on swallowing. In spite of increased ingestion of food the patient began to lose weight and became weaker. The gastrostomy opening was closed, since adequate nourishment could be taken by mouth. Repeated esophagrams showed little evidence of the previous infiltration (Fig. 5, A and B). There was a smooth narrowing through which peristalsis could be visualized fluoroscopically. About the sixty-seventh day after the beginning of treatment a cough developed. This became progressively worse and was followed by dyspnea, râles, and wheezees all over the chest; the temperature rose appreciably. There was clinical and roentgen evidence of bilateral bronchopneumonia (Fig. 5, C and D), and death occurred Aug. 23, 1947, three months after treatment was instituted. No autopsy was obtained.

Comment: This was a far advanced case to begin with and shows how a gastrostomy done too early can defeat the purpose of palliative radiation, since the patient was able to take food up to the time of his death.

CASE III: S. B., a 56-year-old white male, was admitted April 2, 1947, complaining of regurgitation immediately after eating solid foods, of two months duration, and a loss of 38 pounds in three weeks. Esophagoscopy revealed a linear, circular, friable mass almost completely obstructing the lumen. A transthoracic thoracectomy revealed a carcinoma of the esophagus in the upper third above the arch of the aorta, infiltrating into the aortic arch and right hilum and lung. X-ray examination of the lung was negative. Esophagrams revealed a large infiltrative lesion of the esophagus about the junction of the upper and middle thirds.

Treatment: From April 9 to May 7, 1947, the patient received 31,500 r (skin), or a tumor dose of 8,147 r, in 30 days elapsed time and 21 treatment days, through 12 portals. Two portals were treated daily in rotation around the chest. Each portal received 600 r (air); all received three treatments except those more centrally located, which received four treatments.

Course: About two and a half weeks after treatment was begun, the patient was able to eat solid food with ease. He had received by this time a tumor dose of 5,770 r. His weight was stationary. Esophagrams revealed no change in the lesion. There was a definite erythema of the skin. In view of the fact that the tumor seemed more resistant than those previously treated, it was decided to increase the total dose to between 7,500 and 8,000 r. No esophagitis developed. By May 28, 1947, about two and a half weeks after therapy was completed, the patient had gained 3 pounds; he was eating everything; a second degree epidermitis of the skin was healing; there was a slight substernal burning sensation on swallowing. Esophagrams still showed the presence of the tumor, with about 25 per cent regression. Three months after the onset of treatment the weight was stationary and there was no dysphagia. Esophagrams now showed about 40 per cent shrinkage (Fig. 6). Roentgenograms of the lungs at this time revealed slightly increased parahilar infiltration. Five months after the institution of therapy the patient was readmitted to the hospital because of dyspnea and weakness. X-ray studies of the lungs showed an extensive bilateral pneumonitis, more marked on the right. Death ensued on Sept. 9, 1947, five months after beginning of therapy. No postmortem examination was obtained.

Comment: Here the tumor appeared to be more resistant and as a result required a much larger tumor dose before roentgen evidence of regression was obtained. In spite of this large dose, the patient lived longer than any of the others who died.

CASE IV: I. G., a 68-year-old white male, was admitted July 11, 1947, complaining of dysphagia since May 1947 and a 20-pound weight loss during the two weeks before admission. He could swallow nothing but liquids. Esophagoscopy revealed an annular mass, which on biopsy proved to be carcinoma. Esophagrams showed a stenotic infiltrative process of the middle third of the esophagus. X-ray examination of the chest was essentially negative.

Treatment: Between July 16 and Aug. 22, 1947, the patient received a total of 27,320 r (skin), or a tumor dose of 6,300 r, in 38 days elapsed time and 28 treatment days. Each of the 12 portals received 360 r (air) or 460 r (skin) to a total of 1,800 r (air) per portal, except for one anterior and one posterior portal directly over the tumor which received 2,160 r (air) total. Two opposite portals were treated daily.

Course: On the thirteenth day of treatment there was a slight esophagitis. By the twenty-sixth day there was a 5-pound gain in weight. By the end of treatment there was no esophagitis and the patient was on a regular diet. Esophagrams on Sept. 30, 1947, showed a smooth narrowing of the esophagus (Fig. 7), and the patient had gained 22 pounds and returned to work.

Comment: At the last examination, over four months after the initial treatment, there had been no clinical or roentgen evidence of pulmonary fibrosis. Weight had been stationary. This was the first esophagus case to be treated with a smaller daily dose and through opposite portals.

Fig. 7. Case IV: Carcinoma of mid-third of esophagus. A. Esophagram showing marked infiltration. B. Three months after onset of treatment, showing regression and reappearance of esophageal folds in lower half of tumor area.

Of the four patients with carcinoma of the esophagus, one had definite cervical lymph node metastases; in all the disease was well advanced; all had esophageal function restored; one is alive and three died of pulmonary complications.

CARCINOMA OF THE LUNG: CASE REPORTS

CASE V: E. Q., a 51-year-old white male, was admitted Jan. 14, 1947, because of hemoptysis, cough, and pain in the right axillary region radiating to the back, all of two months duration. During that period there had been a 14-pound weight loss. Bronchoscopy of the left main bronchus revealed a mass, and the biopsy report was carcinoma. Fluoroscopic inspiration and expiration studies and films showed an incomplete obstruction of the left bronchus (Fig. 8A). On thoracotomy, a large, hard mass of tumor tissue was found in the curve of the arch of the aorta, extending back from the region of the left main bronchus. It was considered inoperable.

Treatment: Radiotherapy was instituted *via* 8 portals, 300 r (air) to 2 portals a day in rotation. After three days of treatment the temperature rose to 102.4° and the patient refused further irradiation. After eight days, however, the treatment was resumed. By April 15, 1947, after 48 days elapsed time and 28 treatment days, the tumor had received 6,240 r. The total skin dose was 24,000 r.

Course: By the fourteenth day after therapy was begun the chest pain had subsided and there was no further weight loss. By the end of the treatment there was a gain of 6 pounds and inspiration-expiration studies of the chest failed to show any significant shift of the mediastinum (Fig. 8B). There was dyspnea on effort. By October 1947, eight months after initiation of therapy, there was no clinical change; the weight was stationary, and a chest film showed thickening of the left pleura with fibrosis extending from the left hilum to the base. The patient resumed his work as a salesman.

Comment: **When one considers that the average duration of life in untreated cases of carcinoma of the lung from the time the diagnosis is made is three and a half to five months, any increase beyond this time may be attributable to treatment.**

CASE VI: A. M., a 48-year-old white male, was admitted Jan. 28, 1947, complaining of dull pain in

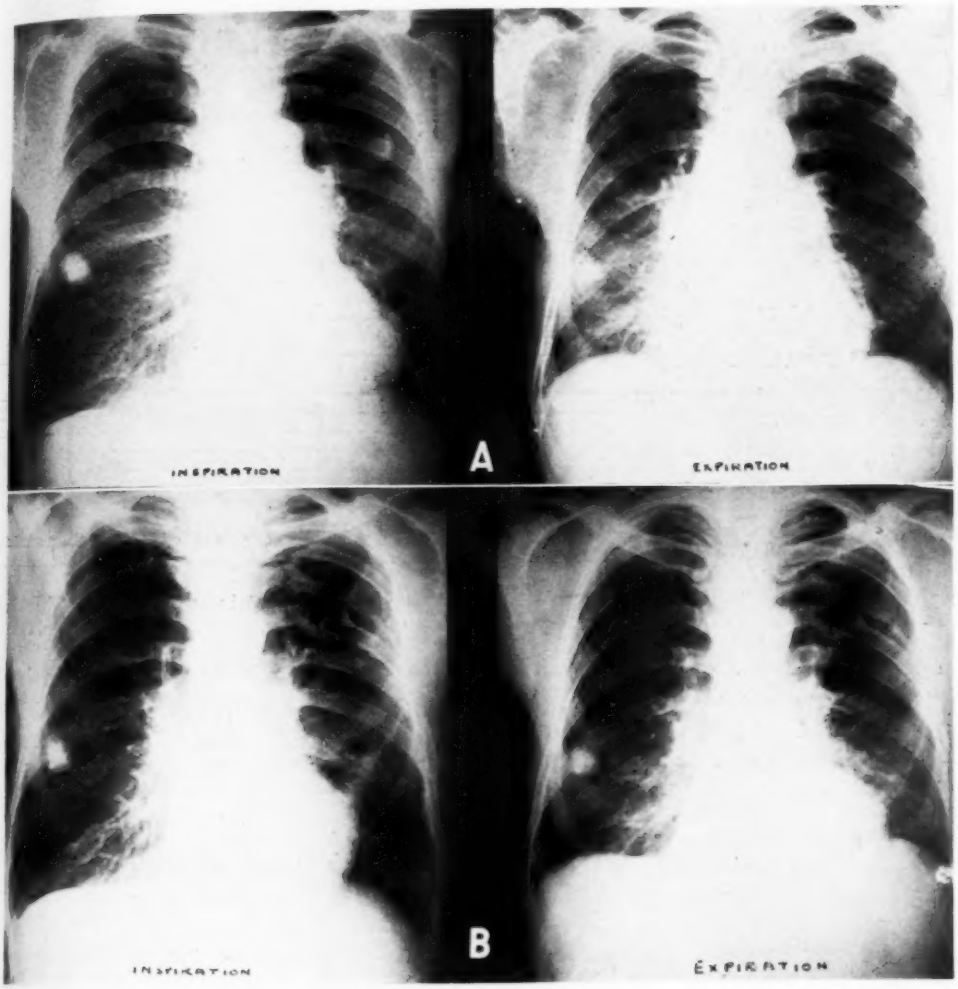


Fig. 8. Case V: A. Inspiration and expiration roentgenograms before treatment, showing shift of mediastinum to left, indicative of partial obstruction at left main bronchus. B. About three and a half months later, showing no shift of mediastinum on inspiration and expiration.

the upper half of the left chest. Bronchoscopy revealed compression of the trachea on the left side, with considerable fixation. A circumscribed area of increased density in the posterior portion of the left upper lobe, extending from the lung root, was demonstrated roentgenologically. A thoracotomy showed the medial portion of the left upper lobe occupied by a large mass which extended to and involved the apex of the lower lobe. Larger nodes were present along the left bronchus to the bifurcation of the trachea. The tumor and nodes, constituted a single mass. It was apparent to the surgeon that this was a carcinoma of the lung with local metastases, which could not be resected. A punch biopsy was done and examination by the Papanicolaou technic led to a diagnosis of anaplastic carcinoma. Following operation, the patient was treated symptomatically, but the pain and discomfort became increasingly severe and he was referred for radiation therapy.

Treatment: From April 23 to May 22, 1947, in a 30-day elapsed time and 16 treatment days, the tumor received 7,562 r *via* 10 portals eccentrically placed. Two portals a day were given 600 r (air) or 750 r (skin) to a total skin dose of 10 × 2,250 r.

Course: By the third week of treatment, the tumor had diminished by 50 per cent. There was no chest pain, but there were dryness in the tracheal region and dysphagia. This was believed to indicate a tracheal epithelitis, and treatment was interrupted

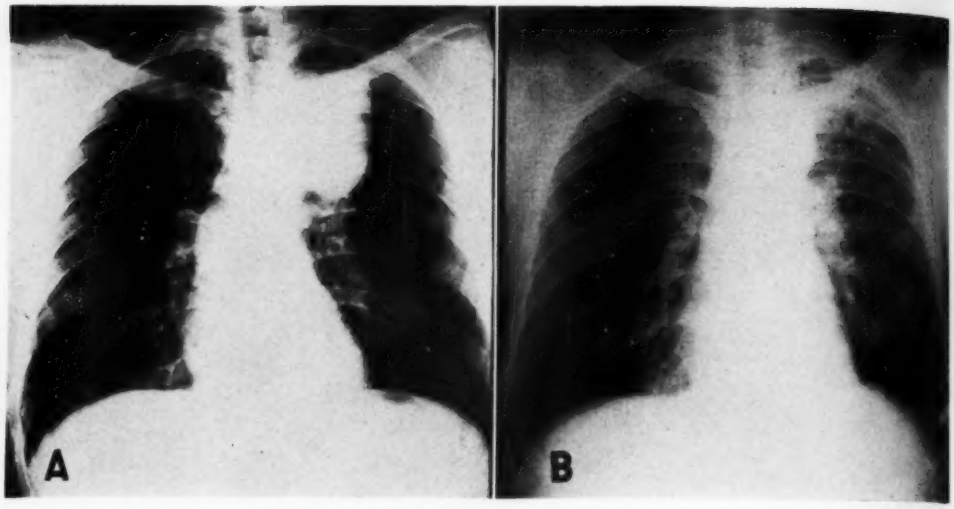


Fig. 9. Case VI: Roentgenograms of lungs (A) before treatment and (B) seven months after treatment, showing marked regression of the tumor.

for about eight days. By the end of treatment the tumor had shrunk 80 per cent (Fig. 9); the patient gained 5 pounds and he has been working since July 22, 1947. He attends the clinic regularly and there has been no further change to date.

Comment; This case received the same intensive therapy that our first three esophagus cases received, without the development of radiation pneumonitis or fibrosis. The fact that this patient was the youngest in the series confirms Freid and Goldberg's (17) contention that elderly persons with arteriosclerotic changes must be considered more likely to suffer such damage.

CASE VII: J. S., a 53-year-old white male, was admitted to the hospital May 21, 1947, complaining of cough, dyspnea, chest pain, and a 15-pound weight loss over a period of seven months. Examination revealed a hard supraclavicular lymph node measuring 2 × 4 cm. X-ray examination of the lungs showed the right upper lobe to be atelectatic. Bronchoscopy revealed marked compression of the right upper lobe bronchus with fixation. At thoracotomy a firm mass about 6 cm. in diameter was found in the right upper lobe, invading the mediastinum. It was deemed inoperable. A biopsy report on the right supraclavicular lymph node described it as metastatic from the lung.

Treatment: The patient received rotation x-ray therapy to the thorax through 10 eccentrically placed portals from Aug. 5, 1947, over a period of 36 days (21 treatment days). Two portals were treated per day in rotation, each receiving 300 r (air). The total for each portal was 1,200 r (air). The skin dose was 15,876 r. The tumor received a total dose of 6,013 r.

Course: After the tenth treatment day, the chest pain had completely subsided and the cough was markedly diminished. At the completion of treatment there were no complaints and the weight was stationary. X-ray examination showed partial clearing of the atelectatic right upper lobe with fibrosis in this region (Fig. 10). The patient has returned to work.

Comment; The fact that the atelectasis has cleared is indirect evidence of tumor shrinkage in this case. In spite of the advanced state of the disease, good palliation has been obtained, there have been no untoward results, and the patient is again at work.

CASE VIII. D. S., a 56-year-old white male, was admitted July 25, 1947, complaining of constant pain in the right shoulder, under the scapula, since February 1947. This was associated with cough and expectoration, but no hemoptysis. A bronchoscopy was done at another hospital and a biopsy of a mass in the right main bronchus led to a diagnosis of squamous-cell carcinoma, Grade II. X-ray examination of the lung revealed a large cavity 6 cm. in diameter between the 5th and 7th ribs in the right paravertebral area. The cavity was irregularly circumscribed in outline, with a fluid level at its base. On thoracotomy, a mass was found in the mediastinum, infiltrating behind the trachea and superior vena cava to the pericardium over the auricle. This was declared inoperable.

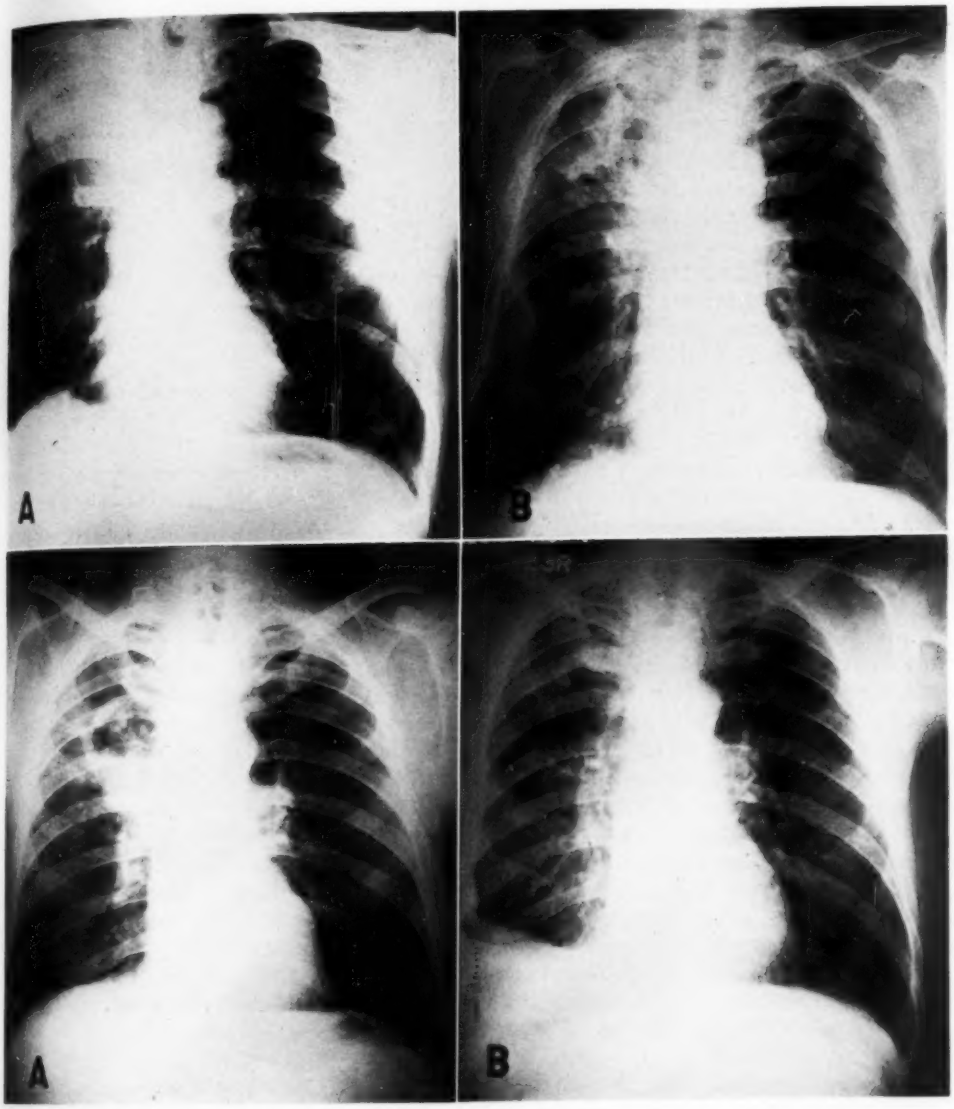


Fig. 10 (above). Case VII: A. Roentgenogram of lungs, showing complete atelectasis of right upper lobe. B. Partial clearing of atelectasis following therapy.

Fig. 11 (below). Case VIII: A. Roentgenogram of lungs showing 6-cm. cavity with fluid level in right upper lobe. B. Roentgenogram made after treatment. The cavity has disappeared, leaving a few fibrotic strands.

Treatment: The patient received rotation x-ray therapy to the thorax through 9 portals eccentrically placed and one special portal angled toward the tumor, the elapsed time being 37 days—July 29 to Sept. 3, 1947—and the number of treatment days 26. Two portals were treated per day in rotation, each receiving 350 r (air), to a total of 1,400 r (air) per portal. The total skin dose was 19,260 r. The tumor received 6,234 r.

Course: When the patient had received 3,089 r to the tumor, on the eighteenth day of treatment, there was some relief of pain in the right shoulder and the cough decreased in severity. By the twenty-first day of treatment the expectoration was greatly diminished and the pain in the shoulder was completely relieved. In two months there had been a gain of 10 pounds in weight and the cavity had disappeared, leaving behind some fibrotic strands (Fig. 11).

Comment: There is no doubt that this was a dramatic result both clinically and radiographically.

DISCUSSION

The response to the first few treatments in each of the earlier cases in the series was most encouraging. Normal esophageal function was restored and roentgenograms taken after the first treatments showed free passage of barium. Unfortunately, the high hopes engendered by these early responses received a check when it was discovered, about three months after treatment was begun, that the patients in our first series were suffering from spasmodic cough, dyspnea, and in some cases expectoration, with roentgen evidence of a diffuse fibrosis of the lungs.

It became evident, after evaluating the results in the first three cases, that the technic would have to be modified if lung injuries were to be avoided. The problem was to find a means of limiting the lung exposure without reducing the number of fields or altering the other important features of the technic. This problem was solved by reducing the daily average tumor dose, administered through two portals, from an average of 250 r (tumor) to 165–170 r. This increased the treatment time from a little over three weeks to about five and a half weeks, permitting the delivery of a tumor dose of approximately 6,000 r, depending upon the circumference of the chest. This change was more in keeping with Strandqvist's good results obtained with 6,000 r in thirty-five to forty days. Another change was to utilize opposite portals in order to avoid the creation of a "hot spot" in front of the tumor, which may result when adjacent portals are treated together. This is especially true as the adjacent portals approach a right angle with each other, and is due to overlapping of the beam, as shown by the isodose curves (Fig. 12).

A treatment period extended too long may result in the development of a connective-tissue reaction without the destruction of all the cancer cells. In addition, the cumulative effect of the radiation is less marked with treatment of short duration than with treatment of long total duration. It is best, therefore, to make the treatment time as short as possible. How far it is possible to go in that respect depends on the general reactions, which are in direct proportion to the dose and in inverse proportion to the duration of treatment.

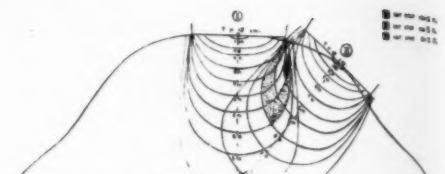


Fig. 12. Dosage distribution of two adjacent ports showing production of a hot spot.

We do not yet possess precise knowledge of the quantitative relationship between dosage and radiation fibrosis. As a result, no simple dosage formulae for lung irradiation can be offered which will prevent the occurrence of fibrosis. The fact that a great many heavily irradiated patients show no recognizable reaction makes us feel certain that we still have a good deal to learn about the way the lung reacts to irradiation. In Widmann's series, only 12 per cent of those patients who received 1,600 to 2,000 r (air) per port had radiation fibrosis (18). Warren and Spencer (19) demonstrated that the amount of radiation alone does not determine the development of a radiation reaction, although the proportion of lungs showing changes increases as the dose is increased.

The possibility of severe injury should be borne in mind if treatment is planned in far advanced cases with palliation as the only aim, so that fibrosis may be avoided. Good palliative effects, characterized by increased ability to swallow and gain in weight, were well established when the

tumor dose reached approximately 3,000 r.

In all of the cases in this series the general reactions were quite similar. The difficulty in swallowing becomes less and less during the course of a week or two of treatment, and the condition gradually improves still further during the course of irradiation. At the end of the treatment swallowing is nearly normal. Esophagrams demonstrate the smooth passage of barium, good mobility of the wall, and natural mucosal relief, with narrowing of the folds. It is obvious that the information afforded by clinical and x-ray examination as to the presence or absence of disease in the esophagus cannot be exact. It is not suggested that even in the most successful cases, in which normal esophageal function has been restored and the x-ray shows a smooth-walled expansile esophagus, some remnants of the disease may not be present. All that can be obtained at this stage is an indication of the condition following treatment. Time will determine whether there has been complete eradication of the disease.

The cutaneous reactions, which did not vary, were moderate, with a marked erythema appearing during the second week of treatment and a dry epidermitis in the third week. In cases where the treatment was completed within twenty-five days, the skin showed blistering epidermitis only one week after the end of treatment. It is suggested that treatment should be completed before a severe erythema has developed, because of the increased radiosensitivity of skin in a state of acute roentgen erythema. During the second and third week of the treatment, at a time when swallowing had already become considerably better, there were some variable complaints of a burning sensation upon swallowing. These dysphagic symptoms were no doubt an expression of an epithelitis of the esophageal mucosa, which usually disappeared in the course of a few weeks.

The general reactions were surprisingly light. In spite of the large daily doses, at no time did the treatment have to be terminated or the dosage altered because of impairment of the general condition, radiation sickness, or increase in temperature. All of the patients were ambulatory and some even put on weight during the course of treatment.

The blood changes were moderate. Two of the cases (one with a higher and one with a lower dose) showed a slight leukopenia, with the absolute number of white cells varying from 3,000 to 5,000 per c.c. No instance of marked leukopenia or marked anemia was observed.

Primary gastrostomy in cancer of the esophagus, as a palliative measure, should be delayed as long as possible, since temporary improvement in swallowing occurs in all cases when the tumor is properly and adequately irradiated. When, however, the obstruction has reached such a degree that even fluids can hardly be swallowed, it is advisable that a gastrostomy be performed before irradiation, since in some cases the radiation reaction may completely close the esophageal lumen and prevent any swallowing.

CONCLUSIONS

Although the small number of cases treated and the short time of observation preclude definite conclusions, it can properly be said that this method of rotation therapy through fixed portals offers definite palliative effects not achieved with any previously employed measures and may in the future provide occasional curative results.

Relief of symptoms occurred in most cases without discomfort to the patients.

The results reported are in accordance with theoretical considerations, and encouraging enough to justify further employment of this procedure.

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SUMARIO

Tratamiento de las Neoplasias Profundas con Técnica de Puertas Múltiples Simulando Rototerapia

Cuatro casos de carcinoma del esófago y cuatro de cáncer del pulmón fueron tratados con una técnica roentgenológica de puertas múltiples fijas irradiadas en rotación. La teoría del método y su empleo en la práctica básanse en el hecho de que el centro hacia el cual se asesta el haz de rayos X quedará expuesto a un tratamiento homogéneo intenso en tanto que cada campo de la superficie cutánea sólo recibirá, debido a la rotación, una fracción de la dosis total. Para los tumores del esófago y del hilio pulmonar se utilizan 12 campos que circundan el tórax; para otros tumores pulmonares se modifica el número de campos de acuerdo con la localización de la lesión.

Cada día se tratan dos campos. Para dirigir con exactitud el haz se utiliza un protractor especial (véase Demy: Radiology **51:** 89, 1948). Los factores de la radiación son: 200 kv., 20 ma., 50 cm. de distancia, filtro de Thoraeus, capa de hemirreducción 1.9 mm. de cobre. La dosis cutánea total administrada durante un período de 23 a 48 días, en 16 a 28 días de tratamiento, varió de 15,876 a 31,500 r. La dosis tumor total se calculó en 5,985 r (en 24 días) a 8,147 r (en 28 días).

Durante el período comprendido en los casos comunicados se descubrió que, para evitar efectos nocivos en los pulmones, convenía rebajar la dosis tumor media por día a 165 ó 170 r entregados por dos puertas. También resultó ventajoso emplear puertas opuestas en vez de adyacentes.

Todos los casos fueron tratados recientemente. Aunque la enfermedad estaba bien avanzada, en todos se obtuvo paliación. En los 4 enfermos de cáncer esofágico se restableció la función esofágica. Tres de estos enfermos han muerto de lesiones pulmonares, a los tres a cuatro meses de aplicarse el tratamiento. Uno se hallaba vivo a los cinco meses y medio sin signos de fibrosis pulmonar. En los casos de cáncer pulmonar también se obtuvo alivio de los síntomas, sin que haya habido muertes en el breve período de observación: dos a ocho meses. Las reacciones cutáneas y generales no fueron intensas.

Rotation Therapy: Theory and Clinical Applications[1]

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ROTATION THERAPY is a technic of irradiating deep-seated lesions by rotating the patient in the beam or by moving the tube about the patient. Within certain limitations this method offers a more symmetrical distribution of radiation and a more advantageous ratio of depth to skin dosage than cross-firing with stationary fields. Although the idea was first suggested in 1906 by Kohl, it was not until 1937 that it was tried. Since 1937 numerous workers, notably Du Mesnil de Rochemont, Dessauer, Jensen, Nielsen and Nakaidzumi, have studied the basic relationships by calculation, measurements on phantoms, and clinical trials on patients.

The object of the procedure is always to have the lesion in the beam while every other part of the body is irradiated only as it passes through the beam on the tube side of the lesion and on the opposite side (Fig. 1). This is easily accomplished by rotating the patient in the erect posture on a simple turntable with the beam horizontal and perpendicular to the axis of rotation. The patient may sit on a stool or stand up, depending upon the part of the body being treated (Fig. 2). Support is rarely necessary. Moving the tube about the patient presents formidable and expensive mechanical problems.

The turntable (Fig. 3) need not be elaborate or expensive. A disk of wood or metal, supported around the edge on roller bearings, and driven by a worm gear and a quarter horsepower motor, is all that is needed. It should be at least 3 feet in diameter and of strong enough construction to accommodate heavy patients. The rate of rotation is immaterial so far as dosage distribution is concerned.

European workers have made elaborate set-ups so that the position, particularly in the treatment of carcinoma of the esophagus, may be continuously controlled by fluoroscopy. They have used very small fields. While such an arrangement may be desirable, it is not, in my opinion, necessary. The small fields offer certain disadvantages, since peripheral parts of a

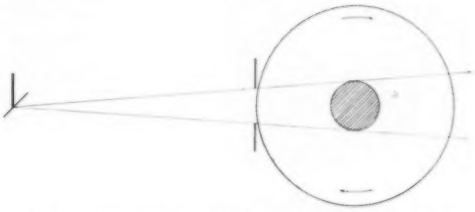

Fig. 1. Diagram of principle of rotation therapy.

lesion, particularly an infiltrating carcinoma, cannot be located accurately. The field, therefore, should be wider than the known lesion. If the patient is turned very slowly, a small change in position will produce a serious disturbance in distribution. If, however, the patient is turned fifteen to twenty-five times during a treatment, a small change in position during one revolution, or part of one, will have little effect. One complete turn a minute is a satisfactory rate. It is slow enough so that the patient does not get dizzy and allows an adequate number of turns per treatment.

The distribution of radiation in the body during rotation is different than with stationary fields. To illustrate this, let us assume an ideal situation, where a cylindrical body is irradiated through a portal which is narrow in proportion to the diameter. The distribution may be represented by a bell-shaped curve (Fig. 4). The greatest amount of radiation is delivered to a cylindrical volume of tissue about the

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Fig. 2. Patient in position for treatment of the lower third of the esophagus.

axis of rotation. With narrow fields, the distribution is practically uniform across this cylinder. At the edge of the beam the amount of radiation received falls off rapidly to a plateau, which gradually descends to the surface. The surface receives the least amount of radiation. Isodose curves are a series of concentric circles (Fig. 5). Under ideal conditions the dose at the central cylinder may be as much as three times that on the surface. During treatment, where ideal conditions cannot always be had, the curve will be modified to some degree, but the basic pattern remains the same.

The shape of the curve and the ratio of deep to surface dosage are altered by changing the width of the field and by changing the shape of the body being irradiated. As the field is widened, the height of the curve, in other words the ratio of the deep to the surface dose, decreases. When the width of the field equals half the diameter of the body, the advantageous ratio disappears and the dose is nearly the same all across the body. In addition to becoming flattened, the top of the curve, representing the part which is continuously in the beam, changes in shape. A slight depression appears in the center of the curve, leaving a slight rise at the edge of the beam. This offers no serious distortion until the field becomes quite wide (Fig. 6).

Fig. 3. The turntable.

Change in the shape of the body causes no material change in the dose distribution about the axis, but alters the height of the peripheral plateau and to some extent the shape of the curve peripherally. In cross sections of the body such as the thorax, which is essentially oval, there is little alteration. The only change is in the skin dose, which is slightly higher along the short diameter. For small fields the amount is negligible and, for larger ones, of only minor significance. In cross sections which are more irregular, such as the pelvis, there is no significant alteration of the central dose. The front and back, along the shorter diameter, receive slightly higher doses than at the sides. There is a little more elevation of the distal limb of the curve on the flatter side of the body, that is posteriorly, so that the back receives a slightly higher dose than the front. As rotation is of particular value where narrow fields in proportion to the diameter

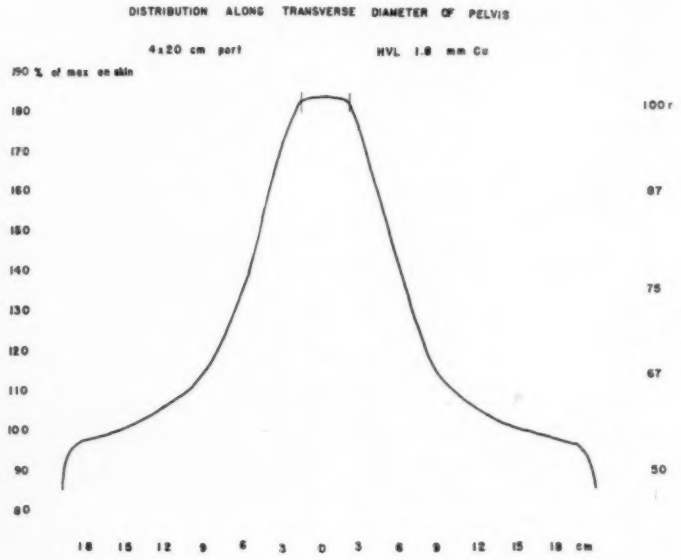

Fig. 4. Distribution curve for narrow port.

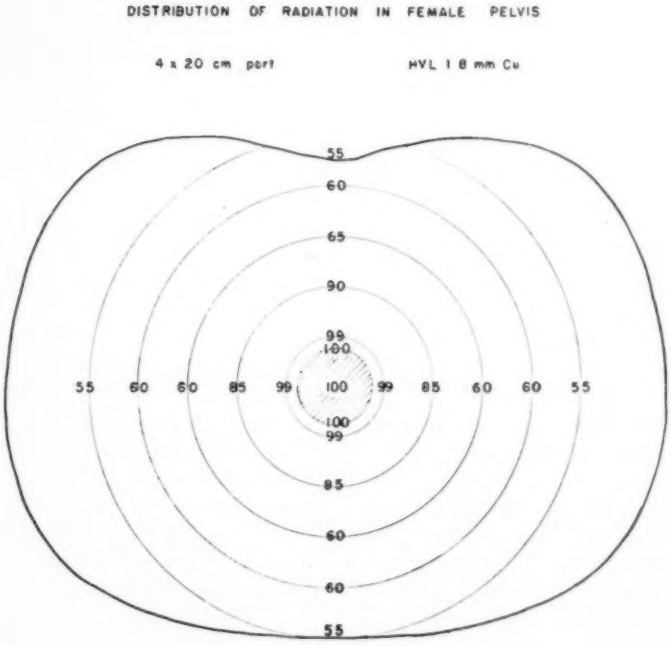

Fig. 5. Isodose curves for narrow port.

can be used, these distortions are not of material significance and may be disregarded. For practical purposes, the body may be regarded as a cylinder having a diameter equal to the average of the actual anteroposterior and lateral diameters.

TABLE I: ROTATION THERAPY. DEPTH AND SKIN DOSES IN PER CENT OF AIR DOSE AT CORE. 1.2 MM. CU H.V.L.

Average Diameter of Part (cm.)	Size of Portal							
	4 × 20 cm.		6 × 20 cm.		8 × 20 cm.		10 × 20 cm.	
	Depth	Skin	Depth	Skin	Depth	Skin	Depth	Skin
16	35.0	19.0	41.0	29.0	45.0	37.0	49.0	45.0
18	29.0	16.0	35.0	26.0	39.0	32.0	43.0	40.0
20	24.0	14.0	30.0	23.0	34.0	28.0	37.0	35.0
22	20.0	12.0	26.0	21.0	30.0	25.0	32.0	31.0
24	17.0	11.0	23.0	19.0	27.0	22.0	29.0	28.0
26	14.0	10.0	20.0	18.0	23.0	20.0	25.0	24.0
28	13.0	9.0	18.0	16.0	21.0	18.0	23.0	21.0
30	12.0	8.6	16.0	14.0	19.0	17.0	21.0	19.0
32	11.0	8.2	15.0	12.0	17.0	16.0	19.0	17.0
34	10.0	7.9	14.0	11.0	15.0	14.0	17.0	15.0
36	9.5	7.6	13.0	10.0	14.5	14.0	16.0	14.0
38	9.0	7.3	12.5	9.5	14.0	12.0	15.0	13.0
40	8.5	7.1	12.0	9.0	13.5	11.0	14.5	12.0

Fig. 6. Distribution curve for wider port.

The absolute dosage is affected by the focus-axis distance, the wave length, and the size and density of the body, as with stationary fields. The depth dose and the ratio of depth to surface dose are better with a longer focus-axis distance and shorter wave length. Table I gives the depth and surface doses in per cent of the air dose. Further tables are being prepared from actual measurements on phantoms of various sizes, for various portals, voltages, and distances, and for various eccentric positions in the body. These tables may be calculated, but experience indicates that calculated values of depth doses and ratios of depth to skin doses are lower than those obtained from measurement.

Several ways of expressing dosage are possible with rotation therapy. The simplest is to use tables similar to Table I. Since the skin dose will always be less than the depth dose, the surface dose becomes secondary and calculations start with the depth dose. Having estimated the tumor size and location, the width and height of the field are determined, and the average diameter of the body at the level of the

tumor is ascertained. The depth and skin dosages can then be readily obtained by a simple calculation from the figures in the table. In a typical case, say a carcinoma of the esophagus in the middle third, let us assume that a field 4 cm. wide is required, and that the patient measures 20 × 30 cm., an average diameter of 25 cm. The depth dose obtained from the table is 15.5 per cent of the air dose and the skin dose at the maximum point is 10.5 per cent of the air dose. Let us decide to give 4,000 r to the tumor in four weeks. Since 4,000 r represents 15.5 per cent of the air dose, 25,800 r in air will be required to deliver the desired dose to the tumor. The highest dose on the skin will be 2,709 r. At five days a week, this will require daily treatments of 1,290 r. This may sound high compared to doses given with stationary fields, but is feasible.

Treatment by rotation has been given to a total of 71 patients. At first, because of the possibility of injury from such a large amount of radiation to large volumes of tissue, small doses only were given. These were gradually raised when no adverse reactions were observed. In the first 20 patients selected, the disease was so far advanced and such small doses were given that they are not included in this report. Of the remaining 51, 36 were treated for carcinoma of the cervix, 8 for carcinoma of the esophagus, 5 for carcinoma of the fundus of the uterus, and one each for carcinoma of the bladder and hemangioma of the brain.

Of the patients with carcinoma of the cervix, 14 received radium therapy also. These were given relatively small doses by rotation, ranging from 1,200 r to 2,550 r to the cervix, with corresponding air doses of 8,000 and 15,000 r. Three were treated five years ago, and 2 have remained well for five years. Three were treated four years ago, and all of these have had recurrences. Eight were treated three years ago, and 2 of this number have shown recurrences requiring further treatment.

The other 22 cases of carcinoma of the cervix were all far advanced and were treated with x-ray by rotation alone. The dosage varied from 1,944 r to 4,032 r to the tumor; 15,000 to 24,460 r in air, in from four to six weeks. While none of this group was cured, palliation was satisfactory by present-day standards.

The 8 patients with carcinoma of the esophagus received from 2,100 to 4,000 r to the tumor; 11,000 to 23,400 r in air. The one who received the largest dose, and was also the most favorable to start with, has remained free from carcinoma as far as can be determined for three years, though he has a cicatricial stenosis at the site of the lesion. In all the other cases there has been a recurrence of the neoplasm.

Of the 5 cases of advanced carcinoma of the fundus, only two received large enough doses to mean much—one 3,600 r and the other 2,400 r to the tumor; 35,700 r and 24,000 r in air, respectively. These two patients were subjectively free from symptoms for one and a half and two years, respectively, though the growth of the cancer subsequently recurred. The others had only short periods of palliation.

The one carcinoma of the bladder treated acted as these lesions usually do. The carcinoma disappeared for a period of eight months and then recurred. This was one of the early cases and the dose was relatively small, 2,000 r to the bladder, 10,100 r in air.

In the case of hemangioma of the brain a gratifying result was obtained. A wide portal was used, equal to half the average diameter of the skull, and 1,000 r were given across the cranium, 6,000 r in air, in a period of four weeks. The dosage figures are calculated, as no measurement has been made on phantoms so small. At the height of the reaction all the patient's hair came out and there was a faint erythema over the cranium. His hair subsequently grew back. He returned to work after three months and remained symptom-free for two years.

While the number of patients treated is not adequate for evaluation in terms of five-year cures, it is sufficient to estimate the effect of rotation therapy on the patient

and to some extent on the disease. The patient tolerates large daily doses without difficulty. Practically all will tolerate 1,000 to 1,250 r daily without symptoms. This is not incomprehensible when it is realized that only a small volume of tissue receives a large dose, and the great volume of tissue receives a small one. Superficial reactions are minimal in spite of the large doses. No evidence of damage to normal tissues has been observed outside of the tumor zone. In cases treated over the pelvis there was only slight bladder and rectal irritation, not at all comparable to that often seen in cross-firing with stationary fields So far, the lesions have not shown materially better results than comparable cases treated by conventional cross-firing methods, though the response is equally good. There is some evidence to indicate that the tumor response was better in the patients who received larger doses.

These observations have been confirmed by other therapists. Nielsen, reporting the largest single series treated by rotation technic, 174 cases of carcinoma of the esophagus, giving air doses ranging from 10,000 r to 50,000 r and tumor doses up to 4,000 r in thirty to sixty days, states that in only 3 cases was there a moist dermatitis of a few days duration. There was no intoxication. No cardiac damage was found electrocardiographically or at autopsy. Pneumonitis and pneumonia appeared in only 3 cases, and in only one of these was this complication severe. No pulmonary changes were found at autopsy. The blood changes were minimal; the hemoglobin was unaffected and the white cells dropped only to 3,000. One patient, aged 74, had osteitis of a dorsal vertebra at the level of the treatment, which was attributed to irradiation.

From my experience with rotation and from the reports in the literature, it is apparent that this technic offers distinct advantages over cross-firing with stationary fields for deep-seated tumors near the mid-line. The results have shown improvement as the dosage has been raised. The maximum safe dosage has not yet been determined. More basic physical measurements are needed to cover various conditions met in actual treatment, and larger numbers of patients will have to be treated with larger doses before the full value of rotation can be determined. Results to the present have been encouraging.

In conclusion, I would like to quote two authors who have had varied and extensive experience. Edling says: "On the whole, it seems that the patients treated by rotation therapy have endured the irradiation with less general discomfort than with corresponding therapy with stationary fields. Such symptoms as nausea, vomiting, and depression have been rare. Anemia and leukopenia as a consequence of treatment do not seem to play any role worth mentioning." And Jensen: "But for anyone who has had any experience with cross-fire treatment of these cases (cancer of the esophagus) it is nevertheless easy to see that the rotatory treatment possesses considerable advantages over the latter; and I and my co-workers know from solidly founded experience that it, in a much larger proportion of cases, can be carried through with considerably less discomfort to the patient and with fewer complications."

SUMMARY

The basic facts of distribution and dosage with rotation therapy have been reviewed. Rotation permits a more even distribution of radiation. The ratio of deep to surface dosage is better than with cross-firing with stationary fields, so that larger doses may be given safely. The efficiency of the method is greater with small fields, longer skin-target distance, higher voltage and smaller patients. Sufficient experience has been gained to show that although a large volume of tissue is irradiated, there is no adverse constitutional effect. There is less damage to normal structures, particularly the skin.

As experience has been gained and the dosages have been increased, results have improved. The maximum safe and successful dosage is yet to be determined.

Rotation therapy offers prospects of improving the results of roentgen treatment of deep-seated lesions.

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SUMARIO

Rototerapia: Teoría y Aplicaciones Clínicas

Al describir una técnica sencilla para la terapéutica de rotación, que utiliza una mera mesa giratoria de madera o metal, preséntase una serie de 51 casos tratados con la misma (36 carcinomas del cuello uterino, 8 carcinomas del esófago, 5 carcinomas del fondo del útero, 1 carcinoma de la vejiga y 1 hemangioma del cerebro). No cabe todavía evaluar los resultados del tratamiento, medidos en términos de cinco años, pero la respuesta de las lesiones, aunque no decididamente mejor, ha sido tan buena como con las técnicas convencionales de fuegos cruzados. Las reacciones contraproducentes han sido mínimas.

La rotación permite una distribución más uniforme de la irradiación. La razón entre dosis profunda y superficial es mejor que con fuegos cruzados en campos estacionarios, de modo que pueden administrarse inocuamente dosis mayores. La eficacia de la técnica es mayor con campos pequeños, distancia foco-piel más larga, mayor voltaje, y enfermos pequeños. La experiencia obtenida es ya suficiente para demostrar que, aunque se irradia un gran volumen de tejido, no hay efecto orgánico nocivo. También se lesionan menos los tejidos normales, y en particular la piel. A medida que ha aumentado la experiencia y se han acrecentado las dosis, el resultado ha mejorado, pero está aun por determinar la máxima posología inocua y eficaz.

DISCUSSION

(Papers by Buschke and Cantril; Nolan and Steele; Leucutia, Evans and Cook; Hawley; Kaplan and Etkin)

Milton Friedman, M.D. (New York City): I am sure we all feel that those members of the Society who have not heard the presentation this morning have missed not only an interesting group of papers but some significant contributions to radiation therapy.

Dr. Buschke has ably defined for us a new lesion that comes into the fold of radiocurability and has shown its resemblance to the majority of radiosensitive carcinomas of the cervix and upper respiratory tract. Apparently its pattern of efficient irradiation falls close to 4,000 r in a period of approximately twenty-five days. It is interesting also to note that Dr. Buschke's average optimum daily tumor dose is approximately 200 r, an important foundation upon which we should build our radiation technics.

Concerning the interesting study of the distribution of radium within the body of the uterus, presented by Dr. Nolan and Dr. Steele, that type of information is extremely important and helpful. I would like to stress one feature, however, and that is that when a linear radium source is pointed at a lesion or portion of the uterus the amount of radiation delivered is small. When multiple capsules are placed in the uterus, those capsules touching the fundus would lie perpendicular to the long axis of the uterine cavity.

Concerning testicular tumors: when we evaluate a group of such tumors, we should divide them into two separate groups. Seminoma, comprising 45 per cent of tumors of the testis, is a very sensitive tumor, having a lethal roentgen dose of 1,000 r delivered over a period of two weeks. The highest percentage of arrested tumors reported from Mayo Clinic is 67 per cent. Even this remarkable figure probably can be improved upon. On the other hand, all the other testicular tumors are virulent lesions with high mortality. A 25 per cent five-year arrest rate may be an exceedingly good result. When we lump them all together, the statistical study loses some significance.

The two papers by Hawley and by Kaplan and Etkin are an extremely important contribution to radiation technic. The multiple field and rotation therapy technics are probably as much as fifteen years old, but those authors who first propounded them did not follow through, and the fact that the essayists have done so, and have acquired enough clinical experience to back their contentions, is a credit to both of them.

In general, I would guess that rotation therapy described by Dr. Hawley may be slightly more efficient than the multiple port therapy with which I am intimately familiar, but there are specific indications for each technic.

Ralph M. Caulk, M.D. (Washington, D. C.): I am particularly intrigued by Doctor Hawley's comments. I would like to ask him one or two questions. It would seem to me, in cancer of the cervix, for instance, that the patient would have to stand erect in order to avoid over-irradiation of the inner aspect of the thigh, particularly the genitocrural region. This suggests another point: Dr. Hawley was able to give 1,000 to 1,200 r measured in air at the level of the skin, daily; I further gathered that the size of the daily dose would depend actually upon the size of the field irradiated. If that is so, a treatment of 1,000 r would require approximately fifty minutes. What are the practical possibilities of a person standing erect for a fifty-minute treatment? I hope Dr. Hawley will answer these questions.

J. C. Cook, M.D. (*closing*): I would like to thank Dr. Friedman very much for his remarks. We also feel that the pathology of these tumors is of great importance in any discussion of prognosis and treatment. Our cases have been referred to us largely from various hospitals in and about the Detroit area and from surrounding Michigan. We found that the classification of the microscopic findings varied almost as much among our local pathologists as it does in the literature. The biopsy specimens from about 50 per cent of our

cases have been collected by us. We hope to gather the rest of the specimens and, following reclassification, prepare a paper in which the pathological classification is given its due importance.

Sydney J. Hawley, M.D. (*closing*): I also would like to thank Dr. Friedman for his generous remarks, and I will attempt to answer the two questions with a little history.

Originally I had a bicycle seat arrangement on a track so it could be moved foward and backward and up and down, the idea being to furnish a central stabilization for the patient. We found that it was quite difficult to center the patient with this device and finally removed it. It is easier merely to have the patient stand in a natural position on the turntable. You first line the patient up with the diameters of the turntable. The tube is previously aligned to the center of the vertical axis. The patient is then rotated two or three times, a pointer being used along the cone to see that he is properly centered. If he wishes, he can stand with feet quite widely separated to steady himself without changing the lateral diameter of the pelvis significantly.

With regard to the time, the period of each application ran from twenty-five to forty-five minutes. In the longer runs, if the patient was uncomfortable, we would stop and give him a rest for a few minutes. This was not often necessary. It is surprising how easy it is to stand still in good position without discomfort.

Calcareous Pancreatitis[1]

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Brooklyn, N.Y.

ONE OF THE LESS frequent causes of upper abdominal pain sometimes disclosed by roentgenographic examination is pancreatitis as manifested by calcific shadows within the pancreas. These may occur as calculi within the ducts, as diffuse parenchymal infiltration, or both types may be coexistent. Diffuse parenchymal calcification of the pancreas is uncommon as compared with pancreatic lithiasis. Beling, Baker, and Marquis (1) stated that approximately 142 cases of pancreatic lithiasis had been recorded up to 1942, of which 13 exhibited disseminated calcification. Snell and Comfort (2) mention that among 54,216 autopsies reported from various sources only 23 instances of pancreatic lithiasis were encountered (2). In 1947, Wirts and Snape (3) were able to collect from the literature but 22 cases of disseminated pancreatic calcification, to which they added 2 of their own. The same year Present and Geyman stated that the literature contained but 17 cases of pancreatic calcification, other than stones, and they, also, reported 2 additional cases (4). Smith and Bonis, however, saw 3 cases in a five-month period (5), and Lüdin noted that stones were found in 28 out of 542 cases examined postmortem when the pancreas was first studied roentgenographically and then carefully dissected (6). The latter observations suggest that careful roentgen examination specifically for pancreatic calcification may perhaps show that the condition is not nearly so rare as believed.

The diagnosis of pancreatic calcification assumes increasing importance in view of the fact that Waugh and his co-workers (7) and Whipple (8) have reported most encouraging results of surgical intervention in patients with pancreatitis who had almost intolerable pain over a long time. Relief of the symptoms associated with pancreatic enzyme deficiencies by means of substitution therapy has been noted by Beazell, Schmidt, and Ivy (9).

We are reporting an additional case of disseminated pancreatic calcification observed for twenty-two months, of interest because of the roentgenologic data and the biopsy obtained during the acute phase of the disease when the calcific deposits were barely visible.

CASE REPORT

M. K., a 39-year-old white woman, had complained of right upper abdominal pain ascribed to gallbladder disease for two years before admission to the hospital. She was the mother of a 15-year-old daughter and the past history was otherwise not contributory.

During the past five months the patient had lost 30 pounds, and a diffuse dull pain was felt in the left upper quadrant. She complained of loss of appetite, but no vomiting. While constipation was the rule, she occasionally had transitory episodes of diarrhea, but nothing unusual was noted in the stool. These attacks lasted about three days and then subsided, leaving a feeling of soreness in the upper abdomen.

The patient appeared chronically ill, thin, and rather apprehensive. A firm, tender, nodular fixed mass about 7 cm. in diameter was present in the left upper quadrant. The liver was not enlarged, and no pain was elicited over the gallbladder region.

The hemoglobin was 75 per cent, with normal blood count. Blood amylase in Somagyi units was 309 against a control of 90, and 200 against a control of 66. Blood lipase was 0.015 against a control of 0 in Comfort units. The blood sugar was 118 mg. per cent. The urea nitrogen, blood proteins, calcium, phosphorus, and alkaline phosphatase were normal. The erythrocyte sedimentation rate was 14 mm. in one hour.

Direct roentgenographic examination of the abdomen on Nov. 8, 1945, showed nothing abnormal at first glance. A barium enema examination five days later showed a smooth depression of the distal third of the transverse colon. Overlying the interspace between the first and second lumbar vertebrae were

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several small discrete calcific shadows, and a similar collection was present just beneath the left twelfth rib. On reviewing the first abdominal roentgenogram the calcific shadows could be identified with difficulty because of the lightness of the film. The barium enema roentgenograms, exposed with a heavier technic, made it possible to see the calcifications even against the density of the spine.

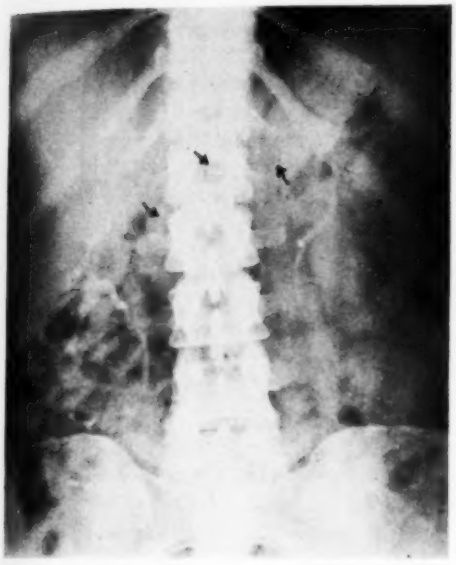

Fig. 1. A few discrete and reticular calcific deposits are present between the right transverse processes of the first and second lumbar vertebrae, in the interpedicular space of the first lumbar vertebra, and between the left twelfth rib and the left transverse process of the first lumbar vertebra (black arrows). Intravenous urography done Dec. 8, 1945.

Roentgen examination of the stomach and duodenum on Dec. 5, 1945, revealed an arcuate impression in the greater curvature of the stomach at the junction of its middle and distal thirds, most constant in the erect position but readily visible in prone projections as well. The gastric mucosa was intact, and the defect was ascribed to extrinsic pressure. The small bowel pattern was not disturbed. On Dec. 8, 1945, one month after the original examination, intravenous urography showed the urinary tract to be normal. The presence of the calcifications was confirmed, and there was an appreciable increase in the number and extent of the calcific shadows. The pattern assumed a reticular appearance, and the disposition of the calcification suggested a diffuse lime salt infiltration of the pancreas. It was noteworthy that with the patient in the prone position the calcifications overlay the right transverse processes of the first and second lumbar vertebrae, while in the recumbent position the shadows were over the second and third transverse processes.

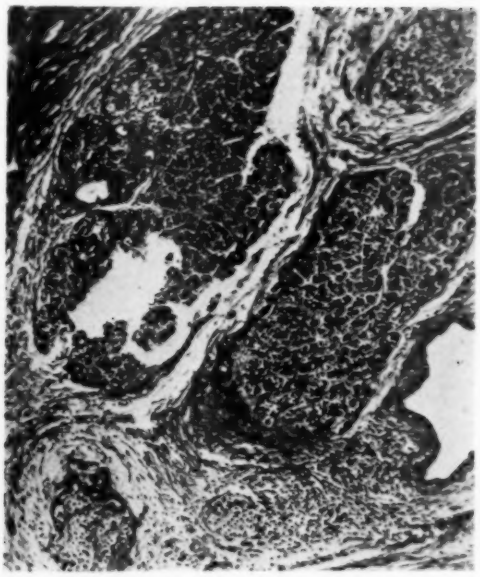

Fig. 2. Biopsy of the body of the pancreas, Dec. 19, 1945, showing perilobular and intralobular fibrosis, leukocytic infiltration, and edema, indicative of acute and chronic pancreatitis.

This, in all probability, is a positional and projectional variation.

At operation, Dec. 19, 1945, the pancreas was found to be from two to three times the normal size, moderately firm and nodular, and so diffusely involved that it was impossible to state whether an inflammatory or neoplastic process was present. The regional lymph nodes were normal and there was no fat necrosis. The gallbladdder appeared normal. A biopsy specimen was taken from the anterior surface of the body of the pancreas. The patient made an uneventful recovery and was discharged ten days later.

Histologic examination of the material removed from the pancreas (Dr. David Grayzel) revealed a marked increase in the perilobular and intralobular connective tissue, with infiltration with small round cells, large mononuclear cells, and polymorphonuclear leukocytes. The tissue was edematous in places, and no atypical proliferation of cells was noted. The acini, ducts, and islet tissues were well preserved. The changes were considered indicative of acute and chronic pancreatitis with fibrosis.

During the next four months the patient had intermittent abdominal pain of varying severity. She continued to lose weight. The mass in the left upper abdomen receded slowly and became less tender. There was no diarrhea. A glucose-tolerance test during March 1946 was normal, and in spite of occasional complaints of excessive thirst, no glycosuria was found. Subsequently the pain became quite

tolerable, the appetite improved, and there was a gain of 10 pounds in weight.

Roentgen examination of the abdomen on Oct. 24, 1946, revealed a pronounced increase in the pancreatic calcifications, the entire organ being outlined with the reticular and discrete deposits. The filling defect in the greater curvature of the stomach had vanished.

The patient returned to the outpatient department during February 1947 and reported that she had had occasional bouts of epigastric pain radiating to the left shoulder and back. The left upper abdominal mass could no longer be felt. During March 1947 she was seen again, the pain having become severe. Roentgen examination again showed the calcification of the pancreas to be extensive.

In view of the continuing severe pain and the obviously poor condition, it was deemed advisable to see if x-ray therapy might afford some relief. This was suggested by a paper by Case, in which it was mentioned that fair results had been obtained in cases he assumed to be chronic pancreatitis (10). Accordingly, between June 10 and July 2, 1947, the patient was given 1,200 r in air to a 10 × 15-cm. portal over the pancreas posteriorly (200 kv., 0.5 mm. Cu and 1.0 mm. Al filtration, 50 cm. distance). This apparently was without effect, as no improvement was observed up to Sept. 5, 1947.

COMMENT

While the causes for pancreatic calcification are not clearly understood, it is generally agreed that the chief predisposing factors include stasis, infection, and inflammation (11). The role of gallbladder disease has not been ascertained, some holding that the entrance of bile into the pancreatic ducts is of etiologic importance (12), while others believe it unlikely that pancreatic lithiasis is necessarily secondary to gallbladder disease (5).

The clinical syndrome is most variable, and it is precisely this indeterminate and fluctuating train of events that prompts radiologic investigation in most cases. Whenever doubt exists as to the cause of abdominal pain, the possibility of pancreatitis should be borne in mind, and proper roentgenographic studies made to rule out pancreatic calcification. In a certain number of patients, presumably those with calculi obstructing the pancreatic ducts, the clinical picture will include steatorrhea, and the gastro-intestinal examination may disclose sprue-like patterns in the small bowel. These cases, of course, should be closely checked for pancreatic calcifications. In a large number of cases, as in the one reported here, no roentgenologic evidence of gastro-intestinal disturbance is obtainable, and the possibility of pancreatitis may easily be overlooked. These patients deserve special examination with carefully focused studies over the upper lumbar area, since even slight calcification in the pancreas may be defined on suitable roentgenograms. In the opinion of Whipple (8), the roentgenologic demonstration of pancreatic calcareous deposits is probably the most important single diagnostic observation available. Confirmatory studies for disturbances of the carbohydrate metabolism and the blood amylase and lipase should also be made.

Goldmann (13) has mentioned that direct examination of the abdomen may show an indistinct mass in the upper part when the pancreas is enlarged. On reviewing the first roentgenogram obtained of our patient, an increase in the soft tissue density in the left upper abdomen, corresponding to the site of the tumor, could be seen. The borders were so indistinct, however, that it would have been hazardous to venture a diagnosis on the basis of this observation alone. The combination of increased soft-tissue density with calcareous deposits in the pancreas may, however, be quite diagnostic.

Rendich, Poppel, and Cove (14), reporting on various lesions of the head of the pancreas, described the formation of pressure defects in the adjacent viscera. This may also be seen with pancreatic cysts, and at times the differential diagnosis might be difficult. However, with the subsidence of the pancreatitis and disappearance of the pressure defects, one may readily conclude that a cyst is not present. The association of a filling defect with pancreatic calcification might be helpful in identifying the process as pancreatitis.

The rate at which pancreatic calcifications develop is not well known. In the case reported here, a slight but nevertheless appreciable increase in the calcific deposits

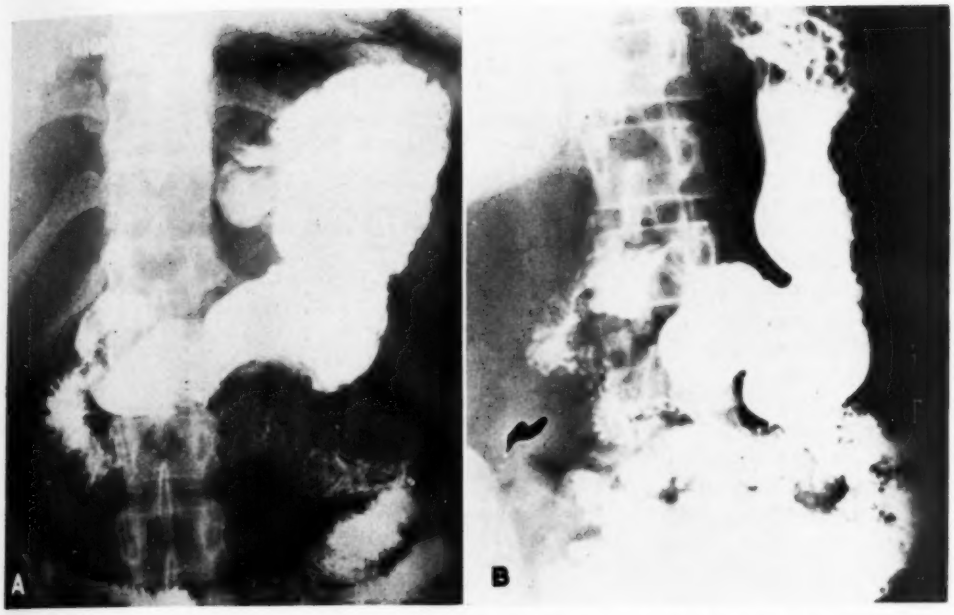

Fig. 3. A. Roentgenogram of the stomach Dec. 5, 1945, reveals an arcuate filling defect in the greater curvature due to extrinsic pressure by the enlarged pancreas. B. Re-examination, Oct. 15, 1946, shows normal configuration of the greater curvature of the stomach. The swelling of the pancreas has subsided.

Fig. 4. A. Roentgenogram, following inflation of the stomach by the use of a Seidlitz powder, March 2, 1947. There has been a marked increase in the pancreatic calcification, so that the entire organ is visualized. B. Lateral examination of the upper abdomen showing position of pancreatic calcifications.

occurred within a month, and ten months later there was a pronounced increase. Darling (15) noted a definite increase in his patient over an eight-month period, and King and Waghelstein (16) reported similar findings in one of their patients over a sixteen-month period. There appears to be no clinical correlation between the initial appearance of the pancreatic calcification, the subsequent rate of development, and the patient's complaints; it is well known that patients with considerable calcification may have little or no discomfort.

SUMMARY

The case history of a 39-year-old woman with acute and chronic diffuse calcareous pancreatitis is presented. Biopsy during the relatively acute stage of the disease showed acute and chronic inflammatory changes. At that time arcuate impressions in the distal portion of the transverse colon and the greater curvature of the stomach, due to enlargement of the pancreas, were seen, and several small calcific deposits were present in the head and body of the pancreas. As the acute phase subsided, the pancreatic calcification increased visibly in one month, and after ten months the entire organ was infiltrated with lime salt. The filling defects in the colon and stomach disappeared as the pancreas became smaller and the calcification increased.

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SUMARIO

Pancreatitis Calcárea

Esta historia clínica es de una mujer de 39 años con pancreatitis calcárea difusa aguda y crónica. Una biopsia ejecutada durante el período relativamente agudo de la dolencia reveló alteraciones inflamatorias agudas y crónicas. En aquella fecha distinguiéronse impresiones arqueadas en la porción distal del colon transverso y la curvatura mayor del estómago, debidas a hiperplasia del páncreas, y había varios pequeños depósitos calcificados en dicho órgano. A medida que cedía la fase aguda, la calcificación pancreática aumentó visiblemente en un mes, y al cabo de diez meses todo el órgano estaba infiltrado con sales cálcicas. Los nichos en el colon y estómago desaparecieron a medida que se contraía el páncreas y aumentaba la calcificación.

Diffuse Pancreatic Calcification

An Analysis of Six Cases[1]

ROBERT J. REEVES, M.D. and FRANK T. MORAN, M.D.[2]

Durham, N. C.

IT INFREQUENTLY becomes the privilege of the roentgenologist to make an absolute diagnosis of pancreatic disease by its direct visualization. He is afforded this opportunity, however, upon demonstrating a pancreas outlined by a diffuse calcium deposition. Beling (2), in 1940, accumulated 12 such cases in a survey of the literature, and added one of his own. Two of the twelve have since been questioned (6). Several subsequent reports have been made (8, 11), and a recent report by Wirts and Snape (12), in 1947, showed a total of 24 cases, including the 2 which they described.

It would appear that diffuse pancreatic calcification is not so rare as it has been previously considered. Recently there have come to our attention several cases presenting diagnostic problems in which the finding of disseminated calcification by the roentgenologist served to confirm the impression of pancreatic disease. Because of this and the relative infrequency of the condition, it was our opinion that a discussion of the subject would be of general interest.

The most common symptom of pancreatic calcification is epigastric pain, variable in severity and character. It is usually intermittent, occasional at first but gradually increasing in frequency and duration. It may be accompanied by nausea and vomiting, weight loss, glycosuria, steatorrhea, and occasionally jaundice. Diabetes mellitus is present in about one half of the cases with diffuse calcification, depending upon the extent of islet damage.

The origin of pancreatic calcium now appears to have been determined. Lymphatic (5) and ascending spread of infection, stasis, and regurgitation from the biliary tract may be contributing factors. Since the patients invariably give a history of symptoms of acute or recurring pancreatitis, the causes classified by Morton (7) are applicable. Edmondson and Fields (5), studying 12 cases of acute pancreatitis, found a marked tendency to mobilization of calcium in the pancreas. In 7 of the 12 cases the serum calcium was subnormal. This may be of value as a diagnostic aid. Trypsinogen and lipase (9) have been incriminated in the process of pancreatic necrosis. Lipase splits neutral fat into fatty acids and glycerin, the acid being deposited and forming soaps (mostly insoluble) with calcium. This was emphasized by Baylin and Weeks (1), who reported a case of acute pancreatitis in which postmortem study showed crystalline fatty acid deposits in numerous areas of fat necrosis.

The diagnosis of diffuse pancreatic calcification is easily made roentgenologically. On a roentgenogram of the abdomen the calcium can be seen to conform to the pattern of the pancreas, extending obliquely from the left upper quadrant downward and across the spine in the region of the second lumbar vertebra. However, involvement may be limited to the head, tail, or body. When not so diffuse, the calcification may present a problem in differential diagnosis. In such cases a lateral film is of considerable assistance. Cholecystography or pyelography may be necessary to rule out gallstones and stones in the kidney. The various aspects of the problem of upper abdominal opacities have been well described by Case (4).

[1] From the Department of Radiology, Duke University School of Medicine and Duke Hospital, Durham, N. C. Accepted for publication in October 1947.

[2] Trainee, National Cancer Institute.

Fig. 1. Case I. The gas-filled stomach affords good contrast for the extensive calcification throughout the pancreas.

CASE REPORTS

CASE I: Mrs. M. L. M., age 33, was admitted to the hospital because of upper abdominal pain, polyphagia, and diarrhea for about five years. She had averaged five to fifteen stools daily, and had frequent nausea. Stools had been variable in color—white, green, and yellow—with a foul odor.

On examination, the blood pressure was found to be 122/88. The urine was positive for sugar. The stools were soft in consistency, clay colored, with the fat content equal to 63 per cent of the dry stool. Blood sugar was 432 mg. per 100 c.c., calcium 7.6 per 100 c.c., and phosphorus 2.5 mg. per 100 c.c. (repeated).

A roentgenogram of the abdomen revealed calcification in the pancreas (Fig. 1). Enzyme studies showed marked diminution of pancreatic enzyme function.

The patient was put on a Schmidt diet and given insulin, liver extract, vitamins, and pancreatin. After the administration of pancreatin there was a diminution of both the fat and nitrogen content of the stool.

CASE II: Mrs. D. C. W., age 29, was admitted because of intermittent right upper quadrant pain for over two years. Six years before admission, she had experienced right upper abdominal pain, nausea, and vomiting. Cholecystectomy was performed at that time, with removal of over one hundred small stones. The symptoms cleared up, but returned three years later.

X-ray examination of the abdomen showed numerous opacities to the right of the first lumbar transverse process, somewhat anterior on a lateral film (Fig. 2). Intravenous urograms were normal.

Exploratory laparotomy showed diffuse calcification in the head of the pancreas.

Fig. 2. Case II: Anteroposterior and lateral roentgenograms showing calcifications in the region of the pancreas. At operation involvement of the head of the pancreas was found to be more extensive than was indicated by the films.

CASE III: J. R. D., male, age 30, was admitted because of severe epigastric pain for eight to ten years, with occasional nausea and vomiting. Careful questioning revealed no probable cause for his illness. Laboratory studies showed an elevated blood sugar and the urine gave a positive sugar reaction (Table I).

A roentgenogram of the abdomen showed extensive calcification in the pancreas (Fig. 3). Exploratory laparotomy revealed diffuse pancreatic involvement.

Because of the intense pain considerable quantities of habit-forming drugs had been used, and the patient bordered on addiction.

CASE IV. J. A. B., male, age 52, was admitted with a history of almost constant epigastric pain for six months and intermittent right upper abdominal colicky pain for six years. He had been a "heavy drinker" until one year before admission. Eight months previous to admission the fasting blood sugar had been 150 mg. per 100 c.c. and the patient had been put on protamine zinc insulin and a diabetic diet.

Gallbladder studies showed poor function. A roentgenogram of the abdomen showed diffuse calcification in the pancreas (Fig. 4).

Operation was deferred

Fig. 3. Case III. The calcifications seen in the upper abdomen were found at operation to be in the pancreas.

Fig. 4. Case IV. The extensive calcification in the region of the pancreas outlines its anatomical position.

CASE V: C. E. W., male, age 33, was admitted because of intermittent epigastric pain radiating to the back for about four years. He had been a heavy consumer of alcohol, averaging two quarts of whisky each week for several years. There had been one episode of delirium tremens.

Fig. 5. Case V. Calcium can be seen throughout the pancreas. The opacities just to the right of the first lumbar vertebra are clips applied during operation.

A roentgenogram of the abdomen showed pancreatic calcification (Fig. 5).

Laparotomy was performed and the pancreas was found to be diffusely indurated, fibrosed, and about once and a half its normal size. Pancreatectomy was deferred and a bilateral celiac ganglionectomy performed, with considerable relief of pain.

CASE VI: M. E. H., a 4-year-old girl,[3] was admitted to the hospital because of recurrent bronchitis with chronic cough and foul smelling, greasy stools for two years. There was no jaundice and the patient had never complained of any abdominal pain. Duodenal drainage was found to be low in pancreatic enzymes.

Roentgenograms of the chest showed some accentuation of the hilar areas and bronchovascular markings, especially at the left base. A film of the abdomen showed a diffuse feathery deposition of calcium throughout the region of the pancreas, and a barium enema study demonstrated dilatation of the sigmoid and colon (Fig. 6).

COMMENT

A review of the 6 cases described above (Table I) shows that 5 patients were less than thirty-five years of age, and all had long illnesses, ranging from two to eight years. The presenting complaint in all of the five adult cases was abdominal pain of

[3] From the Pediatric Service of Duke Hospital. Detailed report awaiting publication.

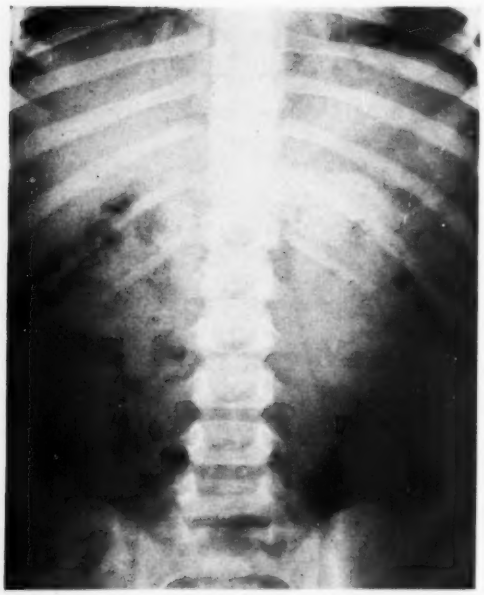

Fig. 6. Case VI, in a four-year-old girl. A light amorphous deposit of calcium is present in the entire region of the pancreas.

varying intensity, mild at first, but increasing in severity and finally causing the patients to seek medical aid. The child had never had abdominal pain. She is believed to be one of the youngest patients with calcified acquired pancreatic disease on record, affording ample proof of occurrence of the condition in children. Two patients gave histories of excessive alcohol consumption for long periods, and in one there had been previous biliary tract disease. The serum amylase and serum lipase were increased in one patient; another had a subnormal serum calcium, possibly indicating an acute episode of necrosis (5).

The roentgenographic finding of calcium within the pancreatic parenchyma is of considerable significance. Since it becomes deposited in areas of fat necrosis, fibrosis, or degenerative tissue, it indicates the site of a pathologic process. It points the way for further clinical investigation and stool, blood and enzyme studies in a patient whose vague type of abdominal complaint may lead to a wrong or incomplete diagnosis. We are well aware of the multitude of conditions brought to mind by the symptom of abdominal pain, and chronic or recurring pancreatitis is one of the most difficult to rule in or out. Pancreatic calcification may indicate the diagnosis.

The gravity of the condition is evidenced by the therapeutic problems presented by the cases reported above. In one patient (Case II), with the least amount of tissue damage as seen on the roentgenogram and at operation, no sequelae were demonstrable. Four of the remaining 5, however, had diabetes mellitus. In addition there were two cases of pancreatic achylia (Cases I and VI), one (Case III) bordered on drug addiction for relief of pain, and another (Case V) had intractable pain for which bilateral ganglionectomy was performed.

In view of the complications attending its progress, it is essential that when early pancreatic calcification is revealed by roentgenogram, all possible therapeutic precautions be taken to prevent further damage. Medically, the treatment varies with the sequelae. In the majority of cases, relief of pain will be the foremost consideration; as has been seen above, drug addiction is an ever-present threat. Diarrhea and steatorrhea may be controlled by pancreatin administration and a low-fat diet; insulin may be necessary to control diabetes. Accessory vitamins are advisable.

Removal of stones from the pancreatic ducts may obviate an ultimately more extensive procedure, and is necessary because of the obstruction and subsequent parenchymal damage they may cause. They may, however, recur. Bost (3) has reported a case in which a stone was removed from the head of a pancreas, and ten years later another from the tail. Calcium once laid down has been found to serve as a focus for further deposition without signs or symptoms of acute necrosis (6). More frequently the repeated attacks of epigastric pain probably represent recurrent episodes of acute pancreatic necrosis.

When the calcification and induration

TABLE I: SIX CASES OF DIFFUSE PANCREATIC CALCIFICATION
SUMMARY OF PERTINENT HISTORY AND LABORATORY DATA

	Case I	Case II	Case III	Case IV	Case V	Case VI
Age	33	29	30	52	33	4
Sex	F	F	M	M	M	F
Presenting symptoms	Abdominal pain; diarrhea	Intermittent right upper quadrant pain	Epigastric pain; weight loss	Epigastric pain	Intermittent severe epigastric pain	Foul smelling stools
Duration	5 years	2½ years	8 years	2 years	4 years	2 years
Predisposing causes	None	Cholelithiasis 4 years previously	None	Considerable alcohol consumption	Chronic alcoholism	None
Jaundice	None	None	None	None	None	None
Blood sugar (mg./100 c.c.)	432	...	300	150	290	104
Stool	63% fat	...	Normal	Normal	Normal	Normal (gross analysis)
Serum amylase	...	Normal	Increased	...	...	Normal
Serum lipase* (N/20 NaOH)	0.6 c.c.	...	3.4 c.c.	...	1.2 c.c.	1.2 c.c.
Serum calcium (mg./100 c.c.)	7.6	...	...	9.2	10.4	9.5
Phosphorus (mg./100 c.c.)	2.5	...	...	2.6	3.7	...

*Normal: 0–1.5 c.c. N/20 NaOH.

are found by roentgenogram and operation to involve only the tail and body of the pancreas, resections of those portions may be accomplished. Where the process is restricted to the head, pancreatico-duodenectomy should be done. A diffuse process throughout the organ, with impaired function and unbearable pain, is an indication for total pancreatectomy with splenectomy and duodenectomy (10). Whipple has reviewed 12 cases of total pancreatectomy from the literature and added two of his own, both for pancreatic calcification (11). The survival time of these patients varied from thirty hours to over three years. Marked relief was noted in those patients who had previously complained of intolerable pain. Constant replacement therapy is necessary following complete extirpation of the pancreas. Celiac ganglionectomy may be efficacious in the relief of pain and is preferable when so extensive a procedure as total removal of the pancreas is contraindicated.

SUMMARY

1. Six cases of diffuse pancreatic calcification are described.

2. Five of the six patients were adults and the chief complaint of each was recurrent abdominal pain of over two years duration. The sixth case was that of a four-year-old girl, believed to be the one of youngest patients with calcified acquired pancreatic disease on record.

3. Two patients gave histories of heavy alcohol consumption and a third had previous cholelithiasis; in the others the etiology was not apparent.

4. The probable pathogenesis and the complications, including steatorrhea, diabetes mellitus, pain, and drug addiction, are discussed.

5. Surgical treatment includes removal of localized concretions, partial and complete pancreatectomy, and celiac ganglionectomy for relief of pain.

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SUMARIO

Calcificación Pancreática Difusa. Análisis de Seis Casos

1. Descríbense seis casos de calcificación difusa del páncreas.

2. Cinco de los seis enfermos eran adultos y el síntoma principal de todos ellos consistía en dolor abdominal recurrente de más de dos años de duración. El sexto caso fué en una niñita de cuatro años, que se considera como la enferma más joven en que se haya comunicado pancreatopatía calcificada adquirida.

3. Dos enfermos comunicaron intenso consumo de alcohol y en otro había antecedentes de colelitiasis; en los otros no había datos etiológicos.

4. Repásanse la patogenia probable y las complicaciones, incluso esteatorrea, diabetes mellitus, dolor y narcomanía.

5. El tratamiento quirúrgico comprende eliminación de las concreciones localizadas, la pancreatectomía parcial o total y la ganglionectomía celíaca para aliviar el dolor.

Iodinated Organic Compounds As Contrast Media for Radiographic Diagnoses

IX. Experimental Studies on the Visualization of the Biliary Tract[1]

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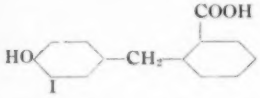
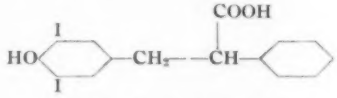
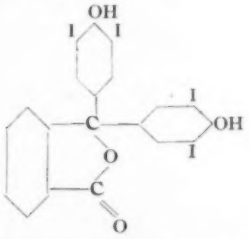
IN THE COURSE OF testing *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid (I) as a cholecystographic agent in dogs, it was observed that the extrahepatic biliary ducts were visualized as well as the gallbladder. Since duct visualization would be a desirable addition to cholecystography, a comparison was made against the standard cholecystographic media to determine whether this property was unique with the benzoic acid derivative. Dogs were used as subjects, and comparisons were made both by oral administration and by intravenous injection.



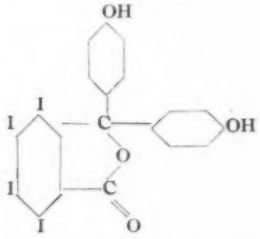
I. *o*-(4-Hydroxy-3,5-diiodobenzyl)-benzoic Acid, 52.9 % Iodine



II. Iodoalphionic Acid (Priodax), 51.5% Iodine



III. Tetraiodophenolphthalein, 61.8% Iodine



IV. Phenoltetraiodophthalein, 61.8%

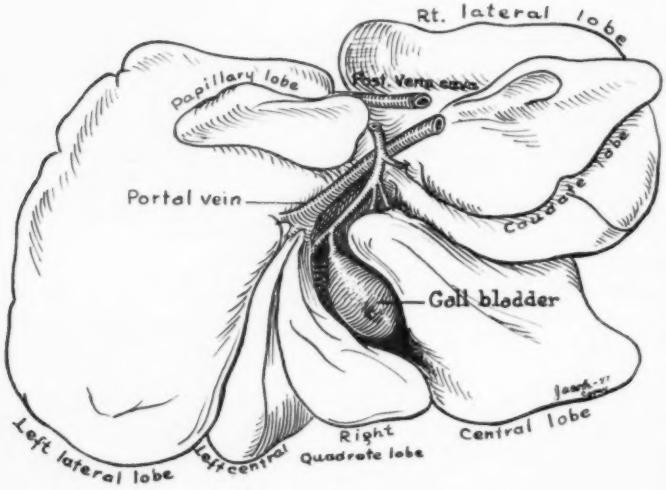
Only the new compound (I) consistently gave good visualization of the extrahepatic ducts after oral administration. Injected intravenously in the form of their sodium salts, the benzoic acid derivative (I), iodoalphionic acid (Priodax) (II), tetraiodophenolphthalein (III), and phenoltetraiodophthalein (IV), all delineated the ducts. There were marked differences, however, in the rate and degree of visualization achieved with each preparation. Delineation was most rapid with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid, and slowest with the iodinated derivatives of phenolphthalein. The time interval for initial duct visualization was in the range of ten to forty minutes.

To eliminate the effect of the gallbladder on the secretion of the cholecystographic media, a number of examinations were made on dogs both before and after cholecystectomy. Intravenous injections of the benzoic acid derivative (I) and of iodoalphionic acid (II) gave satisfactory duct delineation.

ANATOMY

The dog is the most satisfactory of the laboratory animals for the study of chole-

[1] Presented before the Radiological Society of North America at the Thirty-third Annual Meeting, Boston, Mass., Nov. 30–Dec. 5, 1947. This work was aided by grants from the U. S. Public Health Service and from Eli Lilly and Co., Indianapolis, Ind.



A

B

Fig. 1. Anatomical and roentgenological relationships of the extrahepatic biliary system of the dog. A. Sketch of a specimen with the lobes drawn apart. B. Lateral roentgenogram of the biliary tract after retrograde injection with ethyl iodophenylundecylate emulsion.

cystographic media, and is particularly suitable for the investigation of the secretion of such media into the biliary tract.

The liver of the dog is divided into five chief lobes which are separated by deep fissures and drained by three main hepatic ducts. Although *in situ* the lobes overlap, the fresh specimen may be spread out so

that all lobes and the main parts of the extrahepatic duct system are visible, as shown in Figure 1A. The gallbladder lies in a cleft between the two parts of the right central lobe and empties into the middle hepatic duct. The duct system varies greatly from dog to dog, but usually the right hepatic duct drains into the union of the left and middle branches a short distance from the entrance of the common duct into the duodenum.

On roentgenograms the biliary system is best shown in lateral views, with the animal lying on its right side. Figure 1B is a lateral roentgenogram made after the injection of the biliary tract with ethyl iodophenylundecylate emulsion (1). For this illustration 7 c.c. of bile were replaced with 8 c.c. of emulsion through the cannulated common duct of a dead dog weighing 8.2 kg.

EXPERIMENTAL

Subjects: Stock dogs in apparent good health and weighing from 6 to 25 kg. were used in the preliminary studies. Since experience had shown that the biliary systems of the thinner animals are visualized most easily, the comparative series were carried out on two female litter mates which weighed approximately 6.5 kg. each. These year-old dogs are hereafter referred to as dog "A" and dog "B," respectively. The animals were fasted for twenty-four hours before administration of a gallbladder medium, and were rested for about a week before a repeat examination was undertaken with the same or another preparation.

Roentgenography: A precise technic was found to be of critical importance in securing roentgenographic visualization of the gallbladder, the common and the hepatic ducts. A high-speed Potter-Bucky diaphragm, a cone 4 inches in diameter and 15 inches long, intensifying screens, and a 2-mm. focal spot rotating-anode tube at 36 inch distance were employed to give sharp detail and good contrast. The exposure time was kept in the range of 1/30–1/20 second to minimize blurring of the duct shadows.

The dogs were anesthetized with nembutal intravenously before roentgenography. Films were taken with the animal in the anterior-posterior, oblique, and lateral positions. The most extensive and satisfactory visualization of the extrahepatic biliary system was obtained in the lateral position with the animal lying on its right side. All technical factors employed for a particular dog were kept as constant as possible.

Cholecystographic Media: The contrast media used were synthesized or purchased. *o*-(4-Hydroxy-3,5-diiodobenzyl)-benzoic acid (I) was made by the method of Strain (2) and had a melting point of 208–209° C.; the neutralization equivalent was 240. Iodoalphionic acid (II) was obtained by extraction of Priodax pills with chloroform; after purification it had a melting point of 157° C. and a neutralization equivalent of 246 (3). Tetraiodophenolphthalein (III) or its sodium salt and phenoltetraiodophthalein (IV) sodium salt were used as purchased.

Oral Administration: In the initial experimental work three media (I, II, and III) were given perorally. The media were prepared by trituration with 5 to 10 c.c. of 2 per cent arrowroot or cornstarch paste. The dose was administered by washing the suspension through a tube into the stomach with 25 to 50 c.c. of water. The level of dosage varied from 50 to 100 mg./kg. body weight, and in this range the dogs experienced no apparent nausea, vomiting, or diarrhea. The first roentgenogram routinely was exposed sixteen hours following drug administration, but in some experiments earlier films were taken.

At no time was there complete absorption of any of the three compounds from the dog's gastro-intestinal tract. The amount of iodoalphionic acid and of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid absorbed varied from experiment to experiment. Apparently there was little absorption of tetraiodophenolphthalein.

Typical results, obtained with the two litter mates, are given in Table I. In 7 out of 8 examinations *o*-(4-hydroxy-3,5-diiodo-

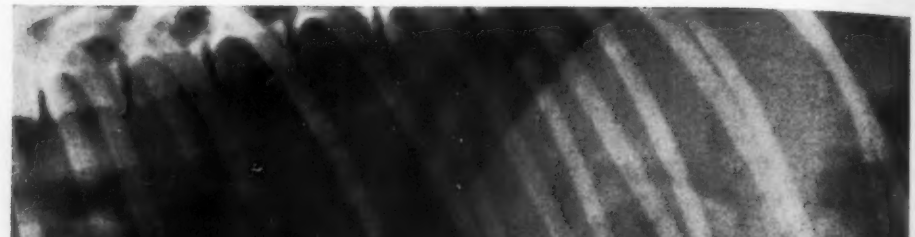


Fig. 2. Visualization of the gallbladder, the hepatic, and the common ducts of a dog twenty-one hours after administration of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid by stomach tube.

TABLE I: BILIARY DUCT SHADOWS SIXTEEN HOURS AFTER ORAL ADMINISTRATION OF CHOLECYSTOGRAPHIC MEDIA TO DOGS*

Medium	Number of Examinations	Examinations Outlining Ducts
o-(4-Hydroxy-3,5-diiodo-benzyl)-benzoic acid	8	7
Iodoalphionic acid (Priodax)	4	1
Tetraiodophenolphthalein	2	0

* Based on an equal number of examinations with each medium, using the litter mate dogs "A" and "B." Dosage level: 50 mg./kg.

benzyl)-benzoic acid visualized the ducts as well as the gallbladder. Iodoalphionic acid outlined the ducts in but one of four studies. Massive oral doses of tetraiodophenolphthalein failed to show even the gallbladder. The cholecystograms obtained at sixteen hours with the benzoic acid derivative and with iodoalphionic acid were of about equal intensity and size.

Almost all examinations with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid outlined the ducts as well as the gallbladder. In some experiments, hepatic duct shadows also could be seen. For one particular study, dog "A" was fasted for the routine twenty-four-hour period and then given the compound by stomach tube at a dosage level of 84 mg./kg. Sixteen hours after drug administration the roentgenogram showed that the intensity of the gallbladder shadow remained the same, but the ducts appeared more intense. In the twenty-one-hour film (Fig. 2) the hepatic ducts also were outlined. Supplementary doses of nembutal kept the dog asleep, and at twenty-two hours two egg yolks were given by stomach tube. The roentgenogram taken thirty minutes after administration of the egg yolks showed a contracted gallbladder and a poorly visualized common duct.

Following oral administration of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid in another experiment, serial roentgenograms were taken every twenty minutes for the first hour, and every thirty minutes thereafter. In this study dog "A" was fasted

twenty-four hours and then anesthetized. After a control film had been taken, the cholecystographic agent was administered by stomach tube at a dosage level of 50 mg./kg. For the first hour the medium was confined to the stomach, but the one-and-a-half-hour film showed that a part of the medium had passed into the small intestine. By four and a half hours none of the medium was left in the stomach. A small portion of the common duct was visualized on the two-hour roentgenogram. The duct shadow increased in extent and intensity on succeeding films, and reached a maximum intensity at three and a half hours. On this film the hepatic ducts also were delineated. The neck of the gallbladder first was visualized five and a half hours after drug administration, and the entire gallbladder was outlined by seven and a half hours. The gallbladder shadow increased in intensity on each successive roentgenogram until the experiment was terminated twelve and a half hours after administration of the cholecystographic agent. Some unabsorbed medium was visualized in the large bowel on the twelve-and-a-half-hour film.

Intravenous Administration: To eliminate the variable of intestinal absorption, the sodium salts of the cholecystographic media were given intravenously at a dosage level of 50 mg./kg. based on the acid. Individual doses of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid and of iodoalphionic acid were prepared by warming the weighed amount of the free acid with a 10 per cent excess of sodium carbonate (calculated to form disodium salt) in slightly less than 10 c.c. of distilled water, filtering, and finally adjusting the volume with distilled water to 10 c.c. Solutions of tetraiodophenolphthalein and phenoltetraiodophthalein sodium salts were prepared from the commercial products by dissolving in distilled water, filtering, and finally making the volume up to 10 c.c.

After the animal was anesthetized with nembutal, intravenously, and placed on its right side, a scout film was taken. Once properly positioned, the dog was not moved throughout the rest of the procedure. Although the external jugular vein sometimes was employed, ordinarily the vein on the lateral aspect of the leg was used for the injections of the solution of the cholecystographic media. Since the same dogs were employed again and again, great care was taken to prevent extravasation of the medium from the veins. Following the control roentgenogram, the solution of the cholecystographic agent was administered over a period of five minutes, and serial roentgenograms were taken at 10-minute intervals from the time of completion of the injection. Most series were terminated at the end of ninety minutes, but some were continued for as long as nine hours. During the longer experiments, it was necessary to give the dogs supplementary doses of nembutal intravenously.

TABLE II: TIME INTERVAL IN MINUTES FOR INITIAL VISUALIZATION OF BILIARY DUCTS AND OF THE GALLBLADDER IN DOGS FOLLOWING INTRAVENOUS ADMINISTRATION OF CHOLECYSTOGRAPHIC MEDIA

Medium	Duct Visualization		Gallbladder Visualization	
	Dog "A"	Dog "B"	Dog "A"	Dog "B"
o-(4-Hydroxy-3,5-diiodobenzyl)-benzoic acid	10	10	20	20
	10	10	20	20
	10	10	20	20
Iodoalphionic acid (Priodax)	60	40	60	30
	10	50	20	50
	60	30	50	70
Tetraiodophenolphthalein	40	50	40	50
	20	20	40	50
	40	30	40	60
Phenoltetraiodophthalein	20	40	60	60
	30	30	70	80

A total of 40 examinations with intravenous injections were carried out, 22 of which were comparative studies on the two litter mates, dogs "A" and "B." In the comparison series the cholecystographic agents were alternated in successive experiments at the same dosage level of 50 mg./kg. The results of the comparison are given in Table II. Although the values for each compound vary somewhat, it is evident that *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid is secreted into the duct system much more rapidly than the other three compounds.

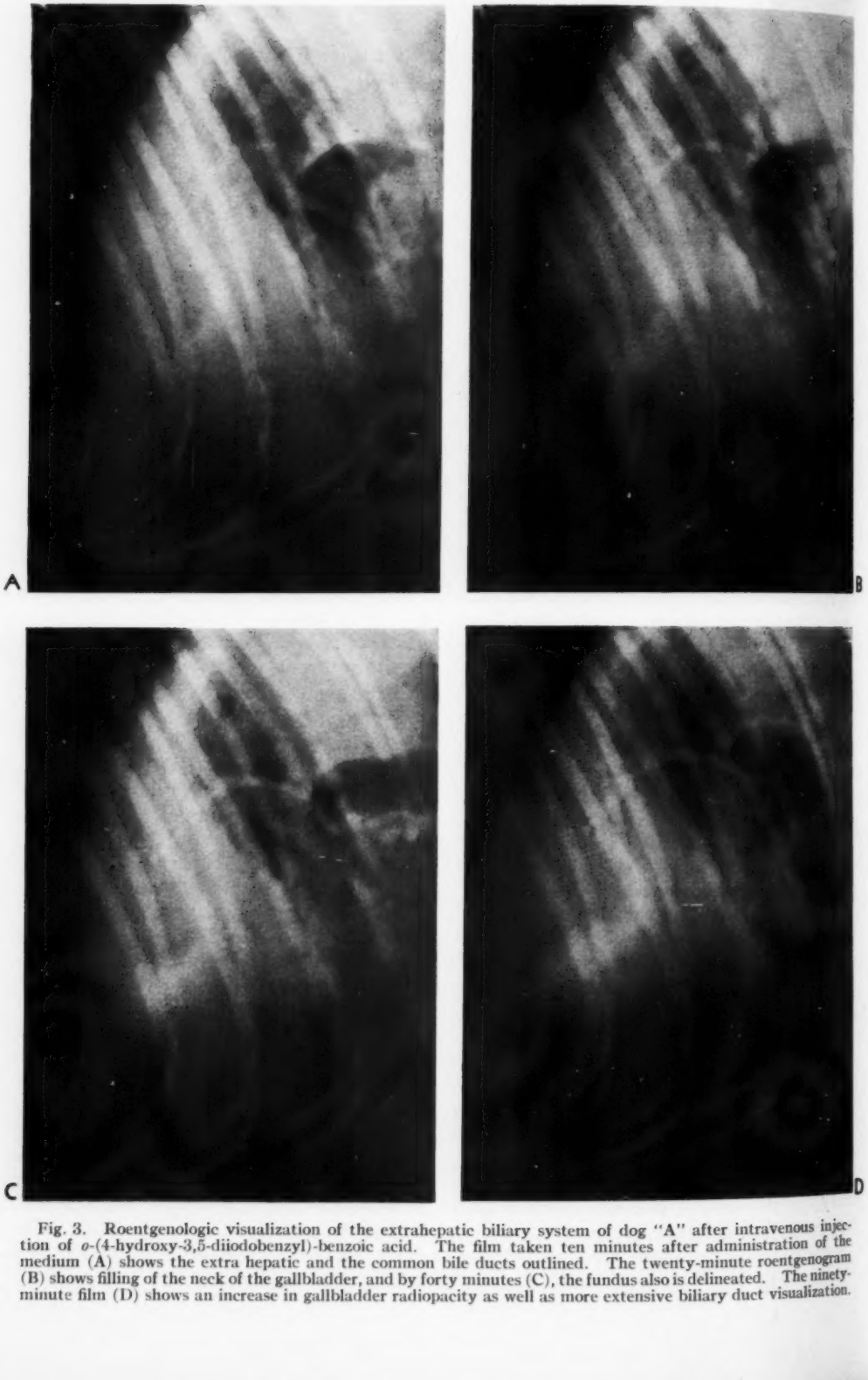


Fig. 3. Roentgenologic visualization of the extrahepatic biliary system of dog "A" after intravenous injection of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid. The film taken ten minutes after administration of the medium (A) shows the extra hepatic and the common bile ducts outlined. The twenty-minute roentgenogram (B) shows filling of the neck of the gallbladder, and by forty minutes (C), the fundus also is delineated. The ninety-minute film (D) shows an increase in gallbladder radiopacity as well as more extensive biliary duct visualization.

On the roentgenograms showing initial duct delineation, the hepatic ducts characteristically were visualized first. Because of the short time necessary for the visualization of the ducts and gallbladder with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid, most of the common duct was outlined on the twenty-minute film, becoming more intense on the thirty- and forty-minute roentgenograms. By the time of the forty-minute film, a number of smaller extrahepatic duct shadows could be seen. Throughout the remainder of the series the common duct shadow maintained its intensity, but became wider, while the opaque media spread from the neck to the fundus of the gallbladder before the shadow became more intense. A typical series after intravenous administration of the benzoic acid derivative is shown in Figure 3.

The duct shadows produced by iodoalphionic acid were less radiopaque and narrower than the shadows produced by the elaboration of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid into the biliary tract Tetraiodophenolphthalein characteristically produced a narrow duct shadow. Although the neck of the gallbladder usually was visualized earlier than with iodoalphionic acid, in three out of six experiments with tetraiodophenolphthalein the entire gallbladder was not outlined by the time the experiments were discontinued at the end of ninety minutes. The visualization obtained with phenoltetraiodophthalein was almost identical with that resulting from tetraiodophenolphthalein.

To determine the effect of cholecystectomy on the roentgenologic visualization of the dog's extrahepatic biliary system, the gallbladders of three dogs were removed after intravenous studies had been completed with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid. Figure 4A illustrates the visualization before cholecystectomy obtained in one dog fifty minutes after intravenous administration of the medium. Five days after the control series was finished, this animal was fasted twenty-four hours and subjected to cholecystectomy by the following technic:

After anesthetization with intravenous nembutal, the peritoneal cavity was entered through a right rectus, vertical, muscle-splitting type of incision. Retraction of the duodenum medialward revealed the gallbladder, the hepatic, and the common ducts. The cystic duct and artery were identified and divided close to the common duct. Care was taken neither to encroach upon the lumen of the common duct nor to leave a stump of cystic duct. The gallbladder then was dissected from the liver bed from neck to fundus with careful hemostasis and attention for potential anomalous bile ducts. The wound was closed in layers with 000 and 0000 interrupted silk sutures, without drainage. On the day after operation, the animal was allowed water and food as desired.

The course after operation was uneventful, and on the tenth postoperative day the animal was anesthetized and given *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid by leg vein. The common and hepatic ducts increased little in opacity. Figure 4B is a reproduction of the fifty-minute film. Throughout the series the ducts appeared markedly dilated. Two months after cholecystectomy another series of roentgenograms was taken, in which the duct shadows appeared as dilated as in the earlier postoperative study. Iodoalphionic acid and tetraiodophenolphthalein given intravenously also outlined the dilated duct system following cholecystectomy.

The other two dogs were studied in similar fashion and comparable results were obtained. The gallbladder of one of these dogs did not follow normal contours when visualized with the gallbladder medium. At laparotomy the gallbladder was found to be bound down by dense adhesions. After cholecystectomy this animal was studied with *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid. In one experiment the animal was fasted for twenty-four hours, and in another it was fed just prior to administration of the benzoic acid derivative. The meal seemed to have no effect upon the extent of visualization or intensity of the common and hepatic duct shadows.

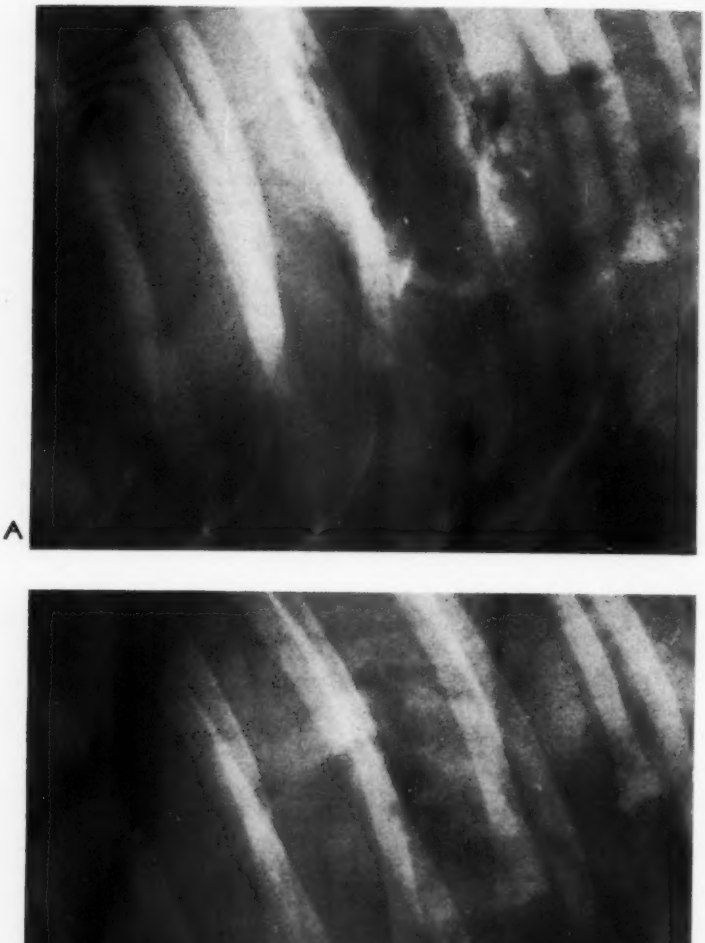


Fig. 4. Roentgenological visualization with intravenous *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid of the biliary system of the dog before and after cholecystectomy. *A*. Film taken fifty minutes after administration of the cholecystographic medium. *B*. Fifty-minute film taken ten days after cholecystectomy.

Iodine Concentration for Visualization of the Extrahepatic Ducts: The concentration of iodine required for the delineation of the extrahepatic ducts was determined by a series of cholangiograms on both living and dead dogs, and by an analysis of a sample of bile obtained ninety minutes after the intravenous injection of the sodium salt of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid. Neither method was entirely satisfactory but both gave the same range of 1 to 2 per cent of iodine as the concentration required for visualizing the duct system by the roentgenographic method used.

For the cholangiograms, aqueous solutions of the sodium salts of cholecystographic agents were employed as well as various dilutions of 50-per cent emulsion of ethyl iodophenylundecylate (1). By the procedure adopted, a laparotomy was carried out on each dog, the duodenum was opened, and the ampulla of Vater cannulated with a blunt No. 17 lumbar puncture needle. The bile was aspirated, and the biliary tract injected with the fluid under study. After waiting five minutes the injected fluid was aspirated, and a second injection was made. The diluting effect of hepatic bile draining from the fine radicles was thus minimized. By this method the ducts were faintly defined when a 1 per cent iodine mixture was used, and definitely delineated by a 2 per cent iodine content.

Mixed bile was aspirated from a dog that died from an overdose of anesthetic ninety minutes after intravenous injection of the disodium salt of *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid at a level of 50 mg./kg. On analysis by one of the iodine methods (4) developed for diodrast, an iodine content of 1 per cent was found. In this case the duct system was as clearly defined as in Figure 3D, but it is uncertain whether the iodine content of the mixed bile was the same as that of the bile in the extrahepatic ducts.

DISCUSSION

That cholecystographic media are secreted into the biliary tract of dogs at a concentration sufficiently great to visualize the extrahepatic ducts on roentgenograms is the significant finding of this study. The retrograde injections into the biliary tract show that an iodine concentration of at least 1 per cent is necessary before the ducts are seen on the roentgenograms, and that the probable iodine content is of the order of 2 per cent. Since the media were administered in the intravenous experiments at a level of 50 mg./kg., and all had an iodine content of 51.5 to 61.8 per cent, the level of the iodine administered was of the order of 25 mg./kg. If the plasma volume of dogs is taken to be 50 c.c./kg., the iodine content of the plasma after injection of each medium is of the order of 0.05 per cent. It follows that a concentration of twenty- to forty-fold takes place as the cholecystographic media enter the biliary ducts. Both the extent and the rapidity with which this concentration takes place are somewhat surprising.

It is difficult by roentgenologic methods to obtain more precise information on the concentration changes that occur in the biliary tract. It is significant, however, that there are definite differences in the type of shadow produced by the several preparations. With the iodinated phenolphthaleins, the delineation of the ducts is least satisfactory and only thin lines of opacity are evident. Somewhat more definite is the delineation obtained with iodoalphionic acid, but the best results are given by *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid. Not only does the iodinated benzoic acid derivative give more complete filling of the duct system, but also the rate of filling is definitely more rapid.

The studies made after oral administration bring out a number of differences in the behavior of the three preparations: *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid (I), iodoalphionic acid (II) and tetraiodophenolphthalein (III). That tetraiodophenolphthalein was not absorbed is explicable on the basis of the high molecular weight (822) and the probable persistence of an anhydride structure during the passage of the medium through the gastro-intestinal tract. The absorption of the other two compounds, I and II, seemed to be about equal; that is compatible with their molecular weights (480 and 496, respectively), and the fact that both compounds contain the same number and kinds of acid groups.

The rate of elimination of the absorbable cholecystographic agents into the biliary tract is probably more rapid than their absorption from the gastro-intestinal tract. This is shown clearly by the experiment in which the benzoic acid derivative was administered orally, and the characteristics of the duct and gallbladder shadows were

followed for a period of twelve hours. After one and a half hours the medium passed through the stomach into the small intestine. At two hours a small portion of the common duct was visualized, and this shadow grew in intensity and extent with the cystic duct and the neck of the gallbladder showing at the end of five and a half hours, and the entire gallbladder at the end of seven and a half hours. During this interval of time not all of the administered medium had been absorbed, and even at the end of twelve hours there was still some of the medium in the large intestine.

The elaboration and concentration of cholecystographic media constitute special problems of gallbladder physiology. Apart from studies on phenoltetraiodophthalein, relatively little work has been done on the rate of disappearance from the blood stream, and still less on the rate of reappearance in the bile. It appears to be generally accepted that a four- to ten-fold concentration of bile takes place in the gallbladder itself (5, 6), but Kirklin, Caylor, and Bollmann (7) did not find a good correlation between bile pigment concentration and the intensity of the gallbladder shadow obtained clinically with tetraiodophenolphthalein. This suggests that the secretion of bilirubin and of the cholecystographic agents is governed by different factors. The studies with the cholecystectomized dogs support this view. After the gallbladders of these animals had been removed, the amount of cholecystographic medium elaborated into the biliary ducts was sufficient for visualization ten minutes after injection. A considerable degree of concentration was necessary to achieve this, and it is improbable that bile pigment concentration took place at the same time. As time passed, however, the intensity of the duct shadow did not increase, and this suggests that the medium was being secreted at a uniform level while bile was escaping through the ampulla. The observations are not good enough to permit more than speculation on this issue, and a great deal is still to be learned concerning the mechanisms and chemistry governing the secretion of cholecystographic media.

With respect to recyclization of cholecystographic media, there are inadequate data. The results of Delario (8) with dogs indicate that tetraiodophenolphthalein after intravenous injection leaves the blood stream in two to four hours; subsequently only a trace of the medium is found in the blood as a result of intestinal absorption. Eitel (9), on the other hand, found that after intravenous injection of tetraiodophenolphthalein there was a gradual decrease of the blood level in normal dogs for ten hours, and that after tying off the common duct the blood level fell off very slowly after an initial drop of 50 per cent during the first hour. In view of the extensive use that tetraiodophenolphthalein formerly enjoyed, it is rather surprising that more work has not been done on the factors involved in the elimination of this medium from the body. In part, this has been due to the fact that the analytical procedures that must be employed are somewhat cumbersome.

This initial study of the secretion of cholecystographic media into the biliary ducts is largely of theoretical interest and does not lead to any immediate recommendations for refinement of clinical roentgenography. The accuracy of clinical cholecystography is high—Scott and Moore (10) report 92.7 per cent and Sosman (11) 95 per cent—yet the failures are frequently in patients where added information is sorely needed. If it becomes possible to make oral or intravenous cholangiograms, the radiological evaluation and surgical attack of biliary tract diseases would be greatly expedited. This would be particularly true in the post-cholecystectomy patient where partial or complete occlusion of the common duct is present from a calculus or inadvertent damage to the duct itself. As Ivy (12) has emphasized, improved media and a better understanding of the physiological factors involved in the filling and emptying of the gallbladder will contribute to this goal.

SUMMARY

Using dogs as experimental subjects, comparisons have been made of the secretion into the biliary tract of the following cholecystographic agents: *o*-(4-hydroxy-3,5-diiodobenzyl)-benzoic acid, iodoalphionic acid, tetraiodophenolphthalein, and phenoltetraiodophthalein.

Administered orally, only the benzoic acid derivative consistently gave good visualization of the common duct. Given intravenously in the form of the sodium salts, all four compounds delineated certain of the hepatic ducts, the common duct, and finally the gallbladder. The most rapid and complete delineation was obtained with the benzoic acid derivative, the ducts being visible ten minutes and the gallbladder twenty minutes after injection. Similarly, the duct system was outlined after cholecystectomy.

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DISCUSSION

Aubrey O. Hampton, M.D. (Washington, D. C.): This paper is so complete that a discussion of the content is not necessary. Its implications, of course, are tremendous. All of us are being asked over and over again, "Why is this patient jaundiced? Is the common duct obstructed or not?" I don't know whether this will solve that problem, but it is at least worth a whirl; a definite trial is certainly in order.

An old and accepted view—I started to call it a theory but I guess it has been proved—is that the reason we see the gallbladder is that the dye is concentrated in it. Why couldn't it be that the gallbladder merely fills with concentrated dye from the liver and thus becomes visible?

The dog, of course, is different from a human being. It seems to be in more than one respect an ideal animal for this study. The relation of soft-tissue density to the size of the common duct looks to be ideal when you think of a big fat patient.

I'd like all of you to know, as I'm sure you do know, that Dr. Strain has already produced one of our best contrast substances, which is being used everywhere, "Pantopaque," and I am certain he is going to produce other contrast substances. As you know, progress in radiology is practically dependent upon these things, so we are very grateful that he has come here to speak to us.

I think when the radiologist is able to control the funds of the x-ray department, he might be able to assist in some of this research by aiding other excellent chemists. I hope some day to be able to offer Dr. Strain a place in my laboratory if he is unhappy elsewhere.

Chairman Rigler: Does anyone else wish to discuss this paper or ask any questions? I am sure Dr. Strain will try to answer any that appear.

Question: Has this medium been tried on any human beings yet?

Dr. Strain (*closing*): As to the clinical test, there is only one patient so far. I have taken half a gram and I planned to take more so that we could answer this question, which I knew would be raised. Unfortunately I had a streptococcus infection which involved my children and myself and I felt that the circumstances were unfavorable to further experimentation. We shall have clinical tests in the very near future.

(*For Spanish summary, see following page*)

SUMARIO

Los Compuestos Orgánicos de Yodo como Medios de Contraste para el Diagnóstico Radiográfico. Estudios Experimentales sobre la Visualización del Aparato Biliar

Con perros como sujetos de experimentación, se hicieron comparaciones de la secreción al aparato biliar de las siguientes sustancias colecistográficas: ácido *o*-(4-hidroxi-3,5-biyodobencílico)-benzoico, ácido yodoalfiónico (Priodax), tetrayodofenolftaleína y fenoltetrayodoftaleína.

Con la administración oral, sólo el derivado del ácido benzoico facilitó constantemente buena visualización del colédoco. Administrados endovenosamente en forma de las sales sódicas, los cuatro compuestos delinearon algunos de los conductos hepáticos, el colédoco, y por fin la vesícula biliar. La delineación más rápida y completa se obtuvo con el derivado del ácido benzoico, quedando los conductos visibles a los diez minutos y la vesícula biliar a los veinte minutos de la inyección. En forma semejante, quedó demarcado el grupo de las vías después de la colecistectomía.

X-Ray Therapy of Boeck's Sarcoid[1]

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IT HAS BEEN generally accepted that sarcoidosis or benign lymphogranulomatosis is a specific disease of unknown etiology, of which uveoparotid fever is just another manifestation (8, 13). Although the etiologic agent is unknown, the tubercle bacillus has been accused most frequently with little direct evidence to support the suspicion that sarcoid may represent a peculiar form of benign tuberculosis. Snapper states that Besnier-Boeck's disease must be considered as a peculiar reaction of the reticulo-endothelium with formation of pseudo tubercles under the influence of an unknown virus (13). The disease runs a chronic, relapsing course and may produce comparatively mild constitutional symptoms but sometimes causes great damage to many structures. Reisner (12) stated that the organs involved, in the order of frequency, were the lymph nodes, skin, bones, spleen, liver, eyes, parotid gland, mucous membrane of the respiratory tract, lacrimal glands, and possibly the serous membranes. Involvement of the nervous system and also of the stomach has been reported. Fibrosis in the lungs may lead to myocardial failure, and lesions in the eye may result in permanent blindness.

Treatment reported by various observers includes x-ray therapy, arsenic medication, ultraviolet and Finsen light, and esters of chaulmoogra oil, none of which has been successful. However, the tendency of the disease to undergo spontaneous regression makes evaluation of any therapy difficult. Roentgen therapy was used by Bernstein and Oppenheimer (1) in 4 out of 6 cases with encouraging results. They felt that the earlier phases of the disease were more likely to respond to x-ray treatment. Katz and co-workers (5) noted a reduction of hilar nodes in one case treated with x-ray therapy. Pohle (11) was impressed especially by the response of the mediastinal lesions to x-ray treatment. However, according to the literature, spontaneous regression is seen most frequently in the pulmonary and mediastinal lesions of sarcoid. Pohle stated that clinical improvement in nearly all cases preceded objective evidence of regression, which appeared two to four months after roentgen therapy was started. He urged radiologists to treat more cases of sarcoid with x-ray in order to determine with greater accuracy the efficacy of this type of treatment.

MATERIAL

Eleven cases of Boeck's sarcoid were treated in the Radiotherapy Department of the Presbyterian Hospital (New York). Of these, 10 were microscopically proved by biopsy. Although no biopsy was obtained on Case 3, the diagnosis was based on the radiological evidence in the chest and hands and on the general course of the disease.

The accompanying table illustrates the inconsistencies of the disease. The ages range from twenty-two to fifty years. Six patients were women and 5 were men. Seven patients were Negroes and 4 were white. Symptoms were varied and, though weakness appeared to predominate, epigastric pain, cough, fever with night sweats, and itching also occurred in occasional instances. Enlarged peripheral lymph nodes were present in 7 patients. Biopsy was done on a lymph node in 6 and on skin lesions in 4 patients.

Enlargement of the liver and spleen appeared infrequently, although Reisner (12) says that pathologically enlargement of the spleen was seen more frequently

[1] From the Department of Radiology of the College of Physicians and Surgeons of Columbia University and the Radiological Service of the Presbyterian Hospital, New York. Accepted for publication in October 1947.

TABULATION OF CASES

Case	Duration of Symptoms	Pulmonary Involvement	Tuberculin Test	Areas of Involvement	Result
1—1927 White Female Age 40	Weakness 72 months	Mediastinal* Peribronchial	...	Liver, spleen, skin	Miliary tuberculosis of lung; tuberculous adenitis Autopsy 1937
2—1932 Negro Male Age 27	11 months	Peribronchial	...	Nodes,* bones, eyes, skin Blood: eosinophils, 16–35%	Unimproved, 1936
3—1934 Negro Female Age 30	Weakness 96 months	Mediastinal*	Neg.	Nodes, bones; neurologic signs	Unimproved, 1942
4—1935 Negro Female Age 25	24 months	Mediastinal* Parenchymal	Neg.	Spleen, eyes, skin*	Unimproved, 1942
5—1936 Negro Male Age 48	Dyspnea 24 months	... ...	... ...	Liver, bones,* skin; neurologic signs Blood: high protein	Chronic care, 1941
6—1938 White Male Age 45	6 months	...	...	Nodes*	Well, 1947
7—1939 Negro Male Age 50	24 months	Mediastinal	...	Nodes,* eyes	Unimproved, 1943
8—1939 White Female Age 26	Weakness 36 months	...	...	Nodes*	Regression. Well, 1944
9—1941 Negro Female Age 30	Iridocyclitis 5 months	Mediastinal* Parenchymal	...	Parotid,* nodes, eyes	Referred to local physician no follow-up
10—1942 White Male Age 22	Weakness Loss of vision 5 months	...	...	Nodes, eyes*	Improved, 1947
11—1942 Negro Female Age 28	Cough, Dyspnea, Iridocyclitis 11 months	Peribronchial	Neg.	Eyes,* skin	Eye degenerated, February 1947

* Areas treated with x-rays.

than could be detected clinically and that it was apt to be found in the early phase of the disease. It is not clear whether Reisner means at autopsy or not. It is of interest to note that the 3 patients in this series who had a palpable liver and spleen did not have enlarged lymph nodes.

Reisner stated that "all patients with bone lesions had skin involvement, suggesting an intimate connection between cutaneous and osseous changes, both being an expression of peripheral dissemination." In our group, 3 patients had bone involvement, only 2 of whom showed skin lesions. A total of 5 patients had skin lesions manifested superficially or by subcutaneous infiltration into the skin.

Many believe that eye and parotid lesions occur simultaneously but it has been stated (12) that eye lesions may occur without parotid involvement. Of our 11 patients, 6 had eye lesions, only 1 of whom had parotid disease.

Seven patients showed involvement of the lungs. The changes were noted most frequently at the roots and usually oc-

curred bilaterally. In this study, only 3 patients had tuberculin tests, all of which were negative.

ROENTGEN THERAPY

The factors used in the roentgen therapy of these 11 patients were 200 kv., 0.5 mm. Cu filtration, 25 ma., and 50 cm. target-skin distance. The areas treated included the lungs, nodes, eyes, and skin. The average total dose was 1,500 to 2,000 r in air, given in daily doses of 100 to 200 r except for the eyes, which received 100 r every other day up to 600 to 800 r in air, with 125 kv., 1 mm. Al filter, 4 ma., and 25 cm. target-skin distance. Occasionally a course of treatment was repeated. Patient 8, who had generalized superficial palpable nodes, received 1,200 r. Eleven months following treatment the palpable nodes were unchanged; within a short time following this examination all nodes disappeared. This was interpreted as a spontaneous regression.

In another patient, Case 7, three subcutaneous nodules of about equal size were given 2,000, 2,500 and 3,000 r in air, respectively. The nodules which received 3,000 and 2,500 r regressed, and the one which received 2,000 r did not. Since the two nodules given the highest dose regressed, the question arises of administering doses in the cancericidal range. Cancericidal doses of x-rays in a chronic, moderately benign disease with the resultant damage to normal tissue does not seem justified at present and particularly in a disease that tends to regress spontaneously. Without irradiation, lesions have been known to heal by hyalinization and fibrosis.

None of the eye lesions responded to roentgen therapy. Patient 10 recovered after an iridectomy. Whether intensive treatment to the uvea, comparable to that in Case 7, would improve the results in the eye cases we cannot say. Such treatment would cause a cataract.

In the 4 cases irradiated over the mediastinum, no regression of the lesions occurred.

SUMMARY

Eleven patients with Boeck's sarcoid received roentgen therapy to various areas, which included the lungs, lymph nodes, eyes, and skin. In one instance skin nodules disappeared after doses of 3,000 and 2,500 r, but another nodule in the same person did not regress with 2,000 r. The lesions of one patient regressed spontaneously eleven months after the conclusion of roentgen therapy. No patient appeared to be clinically benefited by roentgen therapy as far as the course of the disease was concerned.

The number of patients in this series is too small to justify positive conclusions. The results obtained cannot be taken as a recommendation for the use of roentgen therapy as a routine measure in the treatment of Boeck's sarcoid.

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SUMARIO

Tratamiento del Sarcoide de Boeck con los Rayos X

Once enfermos con sarcoide de Boeck recibieron la roentgenoterapia en varias zonas que comprendieron los pulmones, los ganglios linfáticos, los ojos y la piel. En un caso los nódulos cutáneos desaparecieron tras dosis de 3,000 y 2,500 r, pero en la misma persona otro nódulo no cedió a 2,000 r. Las lesiones de un enfermo retrocedieron espontáneamente a los once meses de terminarse la roentgenoterapia. En lo tocante a la evolución de la enfermedad, ningún enfermo pareció beneficiarse clínicamente con la roentgenoterapia.

El número de enfermos en esta serie es demasiado pequeño para justificar conclusiones positivas. El resultado obtenido no puede tomarse como recomendación de la roentgenoterapia como medida sistemática en la asistencia del sarcoide de Boeck.

Unilateral Ureteral Edema Complicating Radium Therapy of Carcinoma of the Cervix

A Case Report[1]

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EXCEPT FOR THE alleviation of pain, a prevalent attitude toward the management of terminal cancer has been, and continues to be, concentrated doses of neglect. The subject of this paper may be said to have received similar attention in the American literature. The sporadic mention which ureteral edema has received has no more than decreased the pain of its presence. The following case report presents the opportunity for a more complete consideration.

CASE REPORT

P. M., a 44-year-old white female, was first seen, by the Tumor Board, on Sept. 26, 1945. At that time she gave a history of increasing vaginal bleeding over a period of six weeks. It had been very severe for the previous three days. She had had no pain nor any menopausal symptoms. She denied any history of pelvic infection, though she did have a mid-line lower abdominal scar.

Physical examination revealed brisk vaginal bleeding with an extroverted mass on the posterior lip of the cervix. The uterus was felt to be mobile and there was no evidence of parametrial thickening. A biopsy of the cervical lesion was reported as squamous-cell carcinoma, grade III.

The following morning radium therapy was begun. This consisted of 3,000 mg. hr. in the uterus, filtered by 0.5 mm. steel; 1,500 mg. hr. by vaginal colpostat with 3 mm. brass and 3 mm. bakelite filtration; 1,500 mg. hr. by vaginal plaque with a filtration of 1 mm. gold and 1 mm. bakelite. The radium capsules used have an inherent filtration of 0.5 mm. platinum. The dosage was divided into four separate applications. The plaque was applied on Sept. 27 and Oct. 8; the intrauterine radium and colpostat together on Sept. 28 and Oct. 9. The patient was discharged asymptomatic on Oct. 11, 1945, with instructions to return for external irradiation on Oct. 24.

On Oct. 18, twenty-two days after the beginning of therapy, the patient was readmitted. On the day following her discharge, sixteen days after the beginning of therapy, she had begun to experience left lower quadrant pain, which did not radiate. The next day she had had the first of daily chills followed by fever. A thick yellow vaginal discharge had also been present since the patient had left the hospital. She again denied any previous pelvic infection, and the examiner was unable to elicit any positive urologic complaints. Physical examination showed bilateral lower quadrant tenderness and a questionable mass in the left lower quadrant. The white cell count was 16,500, with 87 per cent polymorphonuclears.

The patient was placed on penicillin 30,000 units, intramuscularly, every three hours and supportive measures, including vaginal douches twice a day. During the following week her temperature fluctuated between 100 and 103° and she became increasingly toxic. On Oct. 26 the cervical canal was dilated with the expectation of obtaining pus, but none was present. The following day a catheterized urine specimen was negative.

As the patient failed to improve, a gynecologic consultation was obtained, and this was followed by urologic consultation. Cystoscopic examination revealed no anatomic obstruction to the 20-cm. level, but when the catheter was introduced into the left ureter, there was an immediate spurt of cloudy urine which microscopically showed epithelial cells and on culture yielded *Alcaligenes fecalis*. The urologist's impression was ureteritis and pyelitis secondary to edema, which in turn was due to irradiation. The ureteral catheters were left in place for twenty-four hours and irrigated with distilled water every two hours. At the end of that period, the patient's temperature had shown a phenomenal drop and she was feeling much improved, although she still had some lower abdominal tenderness. After Oct. 29 she was completely afebrile.

For the remainder of the course of treatment there was no recurrence of this difficulty and the patient was considered free of disease by both the gynecology and radiology services until July 12, 1946, when the pelvis was found to be "frozen." Only one month had elapsed since her previous clinic visit. In the meantime she had repeatedly complained of swelling of the left leg and persistent left-sided low

[1] From the Department of Radiology, Los Angeles County Hospital, Los Angeles, Calif. Accepted for publication in November 1947.

back pain. She later died of acute generalized peritonitis following rupture of an ulcerative colitis from which she had had no symptoms (Engelbreth-Holm, 4). At necropsy no pathologic lesion was found anywhere in the urinary tract. The cervix showed no evidence of tumor grossly or microscopically, but there were metastases in both parametria, the left ovary (the right had been removed), and the pelvic and para-aortic lymph nodes.

Two major questions had to be settled before it was felt this case could be presented as primary ureteral edema following irradiation. The first: Can the possibility of ureteral edema resulting from pelvic infection be excluded? The second: Could *Alcaligenes fecalis* in the urinary stream produce the whole picture?

There is no final answer to the first question, because of the diffuse involvement of the parametria by metastases at the time of necropsy. It does not seem probable, however, that a previously incurred pelvic infection was responsible, since the former surgery proved to have been only for the removal of an ovary, and the patient so persistently denied any symptoms referable to that system before the onset of the present illness. Furthermore, that a vaginal discharge may occur following irradiation is a widely known fact and this subsided rapidly after the institution of douches and penicillin therapy. This speaks against a new and current salpingitis in previously normal but recently irradiated tissues.

According to Zinsser and Bayne-Jones (13) and Kolmer and Boerner (9), *Alcaligenes fecalis* is almost exclusively a saprophytic organism. Pearson (11) and Gummess (8) state that, if an obstruction has already occurred in the urinary tract, this organism may produce inflammatory changes and do increasing damage so long as the obstruction persists.

In his review of the urologic sequelae of

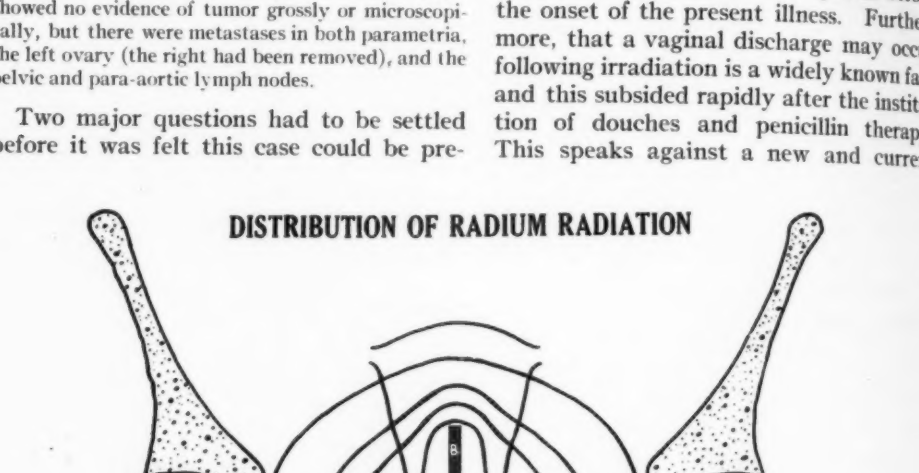

Fig. 1. The location of the ureters is indicated on the border of the zones subject to four to seven and seven to fifteen threshold erythemas. (Adapted from Arneson, A. N.: Radiology **27:** 1, July 1936, by permission of the author.)

irradiation of pelvic organs, Goldblatt (6) quotes the following classification of Dean for bladder reactions: (*a*) a stage of primary erythema, with immediate symptoms; (*b*) a stage of secondary erythema, with symptoms about a month later; (*c*) a stage of tertiary reaction (delayed radium burns), with symptoms a year or more after treatment. Since the bladder and ureter are so closely allied histologically (Bailey, 2) there is no reason to suppose that the ureter should undergo any different type of reaction when exposed to a comparable dose. Martin and Rogers (10) have stated that the ureter does not react to a dose as large as two and a half threshold erythemas. The question arises: To what dose is the ureter exposed during the type of therapy received by this patient? To answer this, an attempt was made to determine the approximate distance of the ureter from the cervix at its nearest point. Several unfixed necropsy specimens were examined by stripping the ureters to the same coronal plane as the center of the uterus. This method is admittedly not exact, since there was considerable stretching of the tissues during this process, but 2 cm. from the external wall of the cervix was finally settled upon as being a satisfactory approximation. As shown in Figure 1, this places the ureters well within Arneson's four to seven threshold erythema zone and possibly within the zone of seven to fifteen erythemas, depending upon the patient, the type of therapy, and the total dosage. This patient received 4,500 mg. hr. by the method illustrated and 1,500 mg. hr. by plaque.

In his excellent article, Arneson (1) states that plaques and bombs can be expected to deliver little to the parametrial areas unless they are placed in the fornices. For this reason it must be considered that the dose to the area of the ureters was somewhat less than that charted here, but it still remains plausible that the ureteral areas in this case received at least twice the dosage quoted by Martin. Such a finding is negative confirmation of Martin's figure, and positive only in the sense that it indicates that the ureter is sensitive to a dosage somewhere between four and seven threshold erythemas. Therefore, the relationship between the cervix and ureters at the time of radium therapy becomes one which is to be regarded with consideration.

Stacy (12) and Chamberlin, Payne, and Stevens (3), have both touched upon this subject, but their references have been to cases in which the ureter is involved in the primary malignant growth by either direct invasion or encapsulation. Furthermore, Chamberlin's case was characterized by the development of complete anuria. Graves and Kickham (7) have definitely pointed out that obstruction may occur from simple edema, but again they appear to depend upon the development of anuria for their diagnosis. Eymer, quoted by Findley (5), has also stated that obstruction may result from edema following irradiation.

DISCUSSION

Upon analyzing the possibilities, it seems unusual that so few cases of ureteral edema following irradiation of the pelvis have been reported in the literature. Furthermore, the reports that do appear are those of cases in which the diagnosis was made when complete anuria had developed.

It is not unlikely that the ureter receives sufficient irradiation during the treatment of carcinoma of the cervix to be subject to a primary radioephithelite. The development of signs and symptoms of an acute pelvic inflammation are not unusual following treatment of these lesions and it therefore becomes a matter for speculation as to whether cases such as the one presented here are not being missed under such a diagnosis. A slight asymmetry of the pelvic soft tissues may have been an underlying influence in this case, where edema appeared to occur on one side only.

Since the human body is never symmetrical, and since most women with carcinoma of the cervix have borne children, which process probably further distorts the pelvic symmetry, the majority of patients would be expected to have one

ureter closer to the source of irradiation, and therefore, more subject to its influence. This consideration makes the probability of unilateral ureteral obstruction from edema a theoretically more common condition than bilateral edema with the development of complete anuria. Since primary edema as a result of irradiation of any tissue is a transient condition, there is no reason to suppose that it could not be completely overlooked under a mistaken diagnosis, with or without coexistent pelvic infection.

That it does occur is proved. Since this is so, it is not to be taken lightly and must not be forgotten in the management of the patient.

SUMMARY

(1) A case of unilateral ureteral edema following radium therapy of carcinoma of the cervix is presented.

(2) The relationship of the ureters to the cervix is considered from the standpoint of possible dosage which the ureters may receive during the course of routine intravaginal and intrauterine radium therapy.

(3) It is pointed out that unilateral ureteral edema may be overlooked under a mistaken diagnosis of reactivation of a pelvic infection.

(4) The literature is reviewed.

(5) A theory as to a possible underlying cause of unilateral ureteral edema is presented.

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SUMARIO

Edema Monoureteral como Complicación de la Curieterapia del Carcinoma del Cuello Uterino. Historia Clínica.

Comunícase un caso en el cual la curieterapia del carcinoma del cuello uterino fué seguida de edema ureteral unilateral. Emprendiéronse estudios de los ejemplares autópsicos para determinar la distancia de los uréteres al cuello en su punto más cercano, obteniéndose una cifra aproximada de 2 cm. Esto indicaría que, con un tratamiento como el administrado en este caso, los uréteres quedarían en una zona expuesta a 4–7 y posiblemente 7–15 dosis eritemáticas según determinara Arneson.

Debido a la asimetría del cuerpo normal y a la deformación del útero que acompaña a la gestación, parece probable que un uréter quede más cerca que el otro del foco de radiación, y teóricamente la ocurrencia de edema monoureteral como consecuencia de la irradiación sería más probable que la de edema bilateral con anuria total. Sin embargo, como se trata de un fenómeno pasajero, se corre el peligro de pasarlo por alto con un diagnóstico erróneo de reactivación de una infección pelviana. No hay que tomarlo a la ligera ni hay que olvidarlo en la asistencia del enfermo.

Carcinoma of the Colon Simulating Carcinoma of the Stomach

A Report of Two Cases[1]

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TWO CASES OF CANCER of the colon in Negro women simulating cancer of the stomach were seen within a period of three months. In each instance the preoperative roentgen examination was incomplete; the stomach and duodenum were studied, but a colon examination was not done. Although in both cases the radiologist felt that gastric carcinoma was the probable diagnosis, barium enema study was recommended to complete the examinations. The surgeons, however, were sufficiently convinced of the diagnosis to operate without this further procedure. These cases are presented to emphasize the importance of preoperative examination of the entire gastro-intestinal tract in patients who have lesions along the greater curvature, if accurate evaluation of the condition is to be made.

CASE REPORTS

CASE 1: M. C., a 49-year-old colored female, was admitted to the Hospital of the University of Pennsylvania on Jan. 9, 1946.

Family History: Negative.

Past History: Surgical menopause (including removal of the ovaries) in 1936.

In 1940, the patient had complained of pain in the epigastrium, nausea, and vomiting. She had noticed no change in bowel habit. Roentgen studies in our clinic at that time were reported negative, but exploratory laparotomy was advised. This the patient refused. (Unfortunately the 1940 films were subsequently destroyed.)

Present Illness: The patient complained of severe chills and fever intermittently and of a mass in the epigastrium for the past three months. She had experienced dysphagia for the past two weeks and could tolerate only liquids; during this time she lost 7 pounds. She vomited intermittently, particularly in the morning, but the vomitus never contained blood. There were no noticeable changes in bowel habit and no gross blood was found in the stools.

Physical Examination: The patient was somewhat undernourished and appeared acutely ill. There was a mass in the epigastrium about 15 cm. in diameter.

Laboratory Report: Gastric analysis positive for occult blood.

Clinical Diagnosis: Carcinoma of the stomach.

Roentgen Findings: There was a large lesion on the greater curvature, extending from the body of the stomach to the pylorus. Fluoroscopically and roentgenographically the lesion seemed to be intragastric in origin. There was no obstruction to the flow of barium through the stomach. The diagnosis was "large lesion of the greater curvature of the stomach, probably malignant" (Fig. 1).

Operation: On Jan. 12, 1946, without examination of the colon roentgenographically, the patient was operated upon. A mass about 5 inches in diameter was found involving the stomach and colon and adherent to the anterior abdominal wall over an area of 1 × 2 inches. The stomach, transverse colon, and spleen were resected. A cecostomy was performed and the appendix was removed. Recovery was uneventful.

Gross examination of the excised specimen revealed a mass which appeared to arise primarily from the colon and to invade the stomach and adjacent fat tissues. The colonic lesion was of the signet-ring variety. It communicated with the stomach through a large necrotic fistula.

Histologically the tumor proved to be an adenocarcinoma arising in the transverse colon.

CASE 2: K. S., a 43-year-old colored female, was admitted to the Hospital of the University of Pennsylvania on April 3, 1946.

Family History: Two sisters had died of tuberculosis.

Past History: Negative.

Present Illness: There had been a weight loss of 10 pounds in two months; loss of appetite and cramping abdominal pains for twelve days. The patient had vomited on three occasions following her noonday meal. There was no blood in the vomitus. Tarry stools were noted only after medication with ferrous iron.

Physical Examination: The patient was somewhat dehydrated. A mass measuring 3 × 5-cm. was palpable in the epigastrium just to the right of the umbilicus.

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[1] From the Department of Radiology of the Hospital of the University of Pennsylvania, Philadelphia, Penna. Accepted for publication in November 1947.

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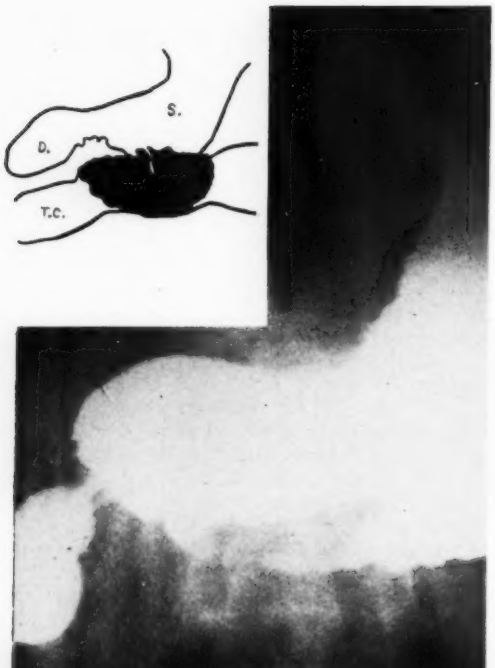

Fig. 1. Case 1. Large filling defect along the greater curvature, produced by a carcinoma of the colon which had extended to and involved the stomach. The diagram illustrates the extent of the lesion (shown in black) as found at operation. The origin of such lesions is difficult to identify unless the colon is studied conjointly or subsequently. *S.* Stomach. *D.* Duodenum. *T. C.* Transverse colon.

Fig. 2. Case 2. The greater curvature of the stomach seemed irregular and the deformity persisted when the patient was placed in various positions during the roentgen examination. An unidentified lesion of the stomach was diagnosed. At operation a carcinoma of the colon was found and an adhesion between the adjacent proximal colon and the duodenum. It is believed that the roentgen appearance was produced by fixation of the colonic mass to the duodenum by the independent adhesion. The diagram illustrates the extent of the lesion (shown in black) and the adjacent adhesion found at operation. *S.* Stomach. *D.C.* Duodenal cap. *C.* Colon.

Laboratory Report: Kline and Kolmer serologic tests positive on one occasion. Gastric analysis positive for occult blood.

Clinical Diagnosis: Carcinoma of the stomach.

Roentgen Findings: There was a mild esophagitis. The stomach was hypertonic and irritable. A deformity of the greater curvature in the prepyloric area was noticed. There was no pyloric spasm and no obstruction to the flow of barium. The deformity was demonstrable in the erect, supine, prone, and Trendelenburg postures. A diagnosis of carcinoma of the stomach or an intramural lesion was made and a barium enema was advised (Fig. 2).

Operation: On April 9, 1946, the morning scheduled for the barium enema, the patient was operated upon. A carcinoma of the transverse colon was discovered and no attachment was found between the colon and the deformity seen in the stomach roentgenographically. A thin adhesion was present between the duodenal cap and the colon adjacent to the lesion.

Histologically there was a carcinoma of the colon limited to the walls of the transverse colon. There was no evidence of carcinoma at the site of the adhesion between the duodenum and colon.

COMMENT

In both of these patients the lesions arose in the colon, close enough to the stomach to produce roentgen findings leading to a suspicion of a gastric lesion. In Case 1, the lesion actually involved the stomach; in Case 2, the lesion in the colon had no attachment to the stomach, but was held firmly against the gastric wall by an

adhesion between the adjacent colon and duodenum. The gastric deformity was apparent only, and not real.

Lesions of the colon are known to involve the stomach in many instances, yet one rarely makes the mistake that was made in these cases. Often the colonic lesion is found by the roentgen examination and the gastric involvement is not suspected. From this experience it would seem that good practice might include a roentgen examination of the colon when one finds a gastric lesion on the greater curvature adjacent to the colon, and roentgen examination of the stomach in patients having a carcinoma of the transverse colon in a region where gastric or duodenal involvement might occur.

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SUMARIO

Carcinoma del Colon Simulando Carcinoma Gástrico. Comunicación de Dos Casos

Descríbense dos casos de carcinoma del colon en los cuales se operó con un diagnóstico erróneo de cáncer gástrico. Ni en uno ni en otro caso se hizo un examen roentgenológico preoperatorio del colon, aunque lo recomendó el radiólogo. En uno la lesión colónica se comunicaba con el estómago a través de una gran fístula esfacelada. En el otro no había comunicación con el estómago, pero la tumoración del colon estaba fijada firmemente contra la pared gástrica por una adherencia entre los adyacentes colon y duodeno.

Sugiérese que una práctica acertada podría muy bien comprender un examen roentgenológico del colon si se descubre una lesión gástrica de la curvatura mayor adyacente al colon y un examen roentgenológico del estómago en los enfermos con carcinoma del colon transverso en una región en la que podría ocurrir invasión gástrica o duodenal.

Kaposi's Disease

Report of a Case with Unusual Visceral Manifestations[1]

KENNETH H. SEAGRAVE, M.D.[2]

KAPOSI'S DISEASE is an uncommon but interesting type of tumor, of low-grade malignancy, which may involve any part of the body. It was first described in 1872 by Moritz Kaposi, after whom the disease was named. The growth is also called, more properly, multiple idiopathic hemorrhagic (pigmented) sarcoma.

Fig. 1. Characteristic pigmented cutaneous nodules of Kaposi's sarcoma. Note the associated edema of the left hand.

The cutaneous manifestations are well known to the dermatologist, characteristically appearing on the extremities as elevated vascular nodules which become pigmented. Visceral involvement is less frequent and usually follows the cutaneous lesions. It may, however, precede them, and Aegerter and Peale (1) have pointed out that the disease may be primary in the viscera with no evidence of skin involvement.

It is the bizarre visceral manifestations of the disease that have aroused particular interest among both clinicians and pathologists. Stats (2) lists the most frequent sites of involvement, excluding the skin in general, as being the glans and preputium penis, the submucosa of the gastro-intestinal tract, the upper and lower respiratory tracts, and the superficial and deep lymph nodes. More unusual locations include serous membranes, spleen, liver, suprarenal glands, myocardium, mesentery, diaphragm, and urinary bladder. A rather comprehensive review of the literature, with particular reference to the visceral manifestations of Kaposi's disease, has recently been made by Tedeschi *et al.* (3).

The case that follows is presented primarily to illustrate some unusual visceral manifestations of the disease, and to add another to the some hundred cases of visceral Kaposi's sarcoma which have already appeared in the literature.

[1] Accepted for publication in November 1947.
[2] Assistant Resident, Department of Radiology, St. Vincent's Hospital of the City of New York.

CASE REPORT

G. M., a 57-year-old Italian male, was admitted to the hospital on Feb. 25, 1947, with a diagnosis of Kaposi's disease. He had been in good health until July 1946, when a mass in the nasopharynx was discovered. Attempts to remove this mass were unsuccessful and resulted in severe hemorrhage. Finally, in November, the lesion was removed and the pathological report was "angiofibrosarcoma of the Kaposi type."

Early in September, several bluish nodular lesions appeared on the palmar surface of the left hand, with similar smaller lesions on the right. In November, lesions developed on the feet, associated with progressive swelling of both legs and of the genitalia. Treatment at the outpatient department of another hospital consisted in roentgen irradiation of the jaw area, several transfusions, and 70 intramuscular injections of non-toxic mustard gas. Despite this treatment, there were progressive generalized weakness, anorexia, and tarry stools. Three weeks before admission ascites developed and a paracentesis was reported to have yielded approximately 8,000 c.c. of fluid. Just before admission there had been hemorrhages of unknown amount from the lower bowel every two or three days. Tenesmus was present. The patient was referred to the hospital for transfusions and further investigation.

Examination at admission showed the patient to be a well developed, middle-aged male, extremely pale and appearing chronically ill. There was marked puffiness about the eyelids; a brownish plaque was noted beneath the left eye. The lymph nodes of the cervical and axillary regions were discretely enlarged and of rubbery consistency; adenopathy of the inguinal areas was even more marked. The abdomen showed bulging of the flank with a questionable fluid wave, but there were no palpable organs or masses. Edema of the scrotum and penis was present; the lower extremities showed a 4-plus pitting edema. The brownish plaques, so characteristic of the skin manifestations of Kaposi's disease, were seen on the flanks, with smaller lesions on the prepuce, glans, and scrotum. The left hand was swollen, and there were several brownish nodules on the palmar surface. The right hand exhibited similar lesions without edema (Fig. 1).

Laboratory studies disclosed an anemia, with a red cell count of 2,000,000 and hemoglobin 40 per cent (5.8 gm.); the blood urea-nitrogen was 24. The total protein was 4.95 gm. per cent with an albumin-globulin ratio of approximately 1:1. Serum bilirubin was 1.1 mg. per cent. Two weeks later it was 1.9, and the Hanger test was 1-plus. The stool was positive for blood.

The patient was given transfusions and other symptomatic treatment. A barium study of the gastro-intestinal tract revealed numerous intraluminal masses, closely clustered together and of varying sizes, in the small intestine (Fig. 2). Signs of a low-grade obstruction were present.

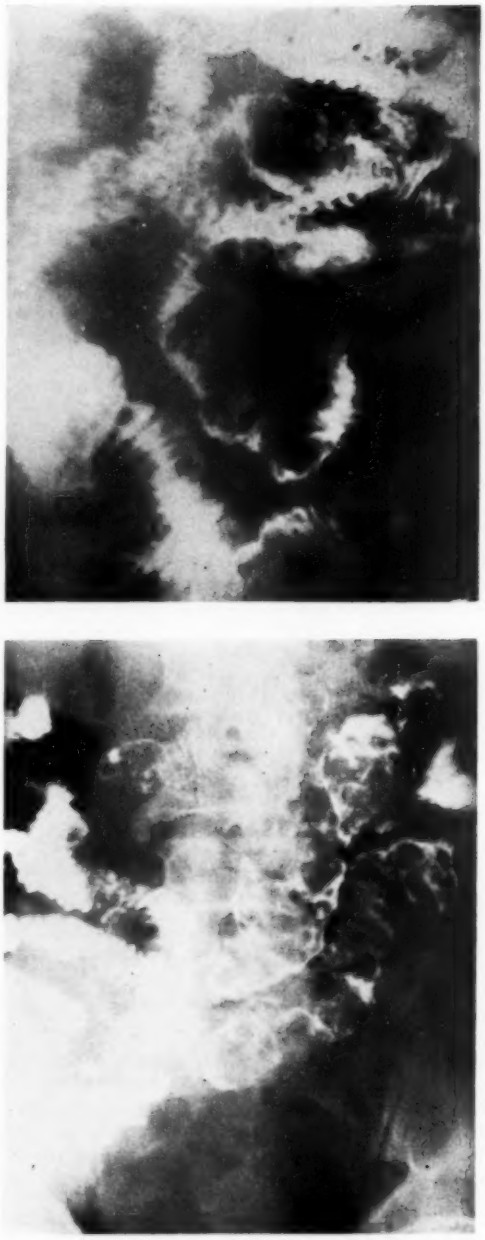

Fig. 2. Roentgenograms at one (upper view) and four hours (lower view) after ingestion of a barium meal, showing large intraluminal masses in the small intestine.

Because of the severe anemia and continued bleeding, surgical consultation was obtained. It was felt that, in spite of the poor outlook, resection offered at least a hope of eliminating the gastro-intestinal

bleeding. At operation, on March 17, 1947, the entire small bowel was found to be involved. The lesions were small in the proximal jejunum and distal ileum, but much larger in the lower two-thirds of the jejunum and proximal ileum. Most of the jejunum and much of the ileum were removed, and a side-to-side anastomosis was performed.

The postoperative course was progressively downhill and death occurred on the fifth day. Permission for autopsy was not obtained.

Pathological examination[3] of the 14 feet of resected small intestine showed large blackish-red polypoid masses, ranging in size from 0.5 to 6.0 cm. in diameter, projecting into the lumen of the bowel (Fig. 3). There were 44 gross lesions counted in the resected specimen, 23 of them being concentrated within 18 inches of bowel. The lesions were irregular, moderately soft, and had a fungating appearance, some undergoing ulceration. On section, the masses were slightly friable and were deep red in color. Numerous areas on the mucosa of the intestines showed hemorrhagic discoloration. In addition to the polypoid lesions, there were numerous purple-red nodules lying completely beneath intact mucosa and ranging up to 1 cm. in diameter. On section they presented the same gross appearance as the larger polypoid masses.

Microscopic sections taken from various portions of the bowel showed the smallest of the nodules to lie in the submucosa. From there they extended in both directions, compressing the mucosa on one side and the muscularis on the other. The tumors were composed of intertwining masses of spindle-shaped cells very closely adjacent to one another. In one of the nodules, superficial, widely dilated channels filled with blood were found, and there was hemorrhage adjacent to this in the surrounding tissue. The diagnosis was Kaposi's disease of the small intestine.

A lymph node from the leaves of the mesentery appeared enlarged due to edema and lymphoid hyperplasia. A skin biopsy showed one small nodule 3 mm. in area, which was slightly raised and pinkish-red in color. On section the tissue was firm, homogeneous, and pinkish-gray in color. The microscopic diagnosis was Kaposi's disease of the skin.

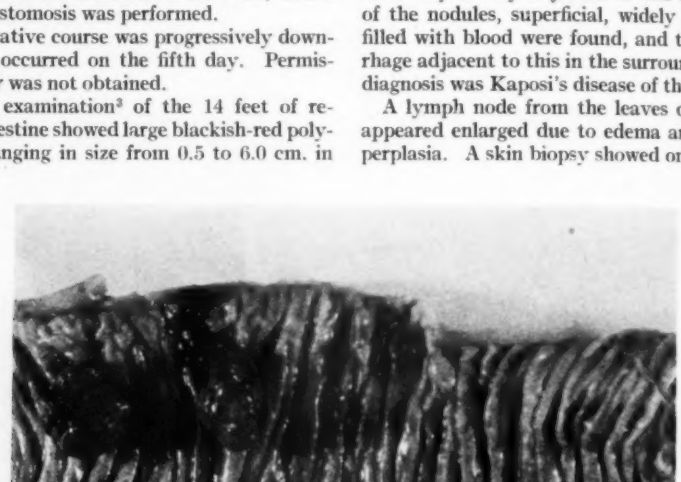

Fig. 3. A portion of the resected small intestine showing polypoid masses of Kaposi's sarcoma projecting into the lumen of the bowel.

[3] By Anthony Rottino, M.D., pathologist, St. Vincent's Hospital.

COMMENTS

Several features of this case are of particular interest. The presenting lesion was in the nasopharynx and, when disturbed, showed excessive bleeding. Stats (2) has pointed out that a hemorrhagic tendency has been described in certain cases of this disease. The frequent occurrence of edema of the extremities in Kaposi's disease has likewise been stressed (2). Generalized lymphadenopathy and unexplained gastro-

intestinal bleeding are two additional features which should serve as a reminder to consider visceral Kaposi's disease in the differential diagnosis of a host of conditions with similar abnormal findings.

There is considerable uncertainty as to the true nature of Kaposi's disease. It has been looked upon as an infectious granuloma and as a true neoplasm. Although the latter view seems more generally accepted, there is still lack of agreement as to the origin of the tumor and its relative malignancy. Aegerter *et al.* (1), in a critical survey of Kaposi's sarcoma, express the opinion that the disease is a vascular cancer—an angiosarcoma, and they regard the secondary visceral lesions as true metastases.

Tedeschi *et al.* (3) advance the concept that Kaposi's disease "is systemic in nature and likely to involve independently and in an unpredictable manner, simultaneously or successively, the skin and the internal organs and that it is characterized from the histologic standpoint by a great variety of patterns inherent to the multiple developmental potentialities of the basic unit of growth, the reticulum cell." There is no way of ascertaining whether or not the varied manifestations in the case just reported represented spontaneous primary multicentric growths or true metastases. A complete autopsy might well have revealed other sites of invasion, and possibly have given some insight into the origin of the disease. Regrettably this could not be obtained, and the case must rest on the unusual antemortem findings.

SUMMARY

A case of Kaposi's disease is presented in which multiple sites of involvement included an initial growth in the nasopharynx, followed by the appearance of characteristic skin lesions and later by evidence of devastating gastro-intestinal invasion. A gastro-intestinal series showed intraluminal masses throughout the small intestine which proved to be polypoid growths of multiple hemorrhagic sarcoma. Illustrations of the skin lesions, as well as roentgenographic and pathologic findings of the visceral involvement, have been included.

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SUMARIO

Enfermedad de Kaposi. Comunicación de un Caso con Extrañas Manifestaciones Viscerales

Preséntase un caso de enfermedad de Kaposi en el cual los muchos sitios afectados comprendían la tumoración inicial en la nasofaringe, seguida de la aparición de típicas lesiones cutáneas y más tarde de devastadora invasión gastrointestinal. Una serie de radiografías gastrointestinales reveló en toda la luz del intestino delgado tumefacciones que resultaron ser tumores polipoideos de sarcoma hemorrágico múltiple. El trabajo comprende grabados de las lesiones cutáneas, así como los hallazgos radiográficos y patológicos de la invasión visceral.

Report of a Case of Hydrometrocolpos—A Congenital Dilatation of the Female Genital Tract[1]

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AN APPARENTLY normal, well developed female infant was delivered after an uneventful labor. The prenatal course of the mother was not remarkable, and she showed no clinical evidence indicative of hormonal imbalance.

Shortly after the infant's birth, it was observed that she voided infrequently, and then only in scanty quantities. During an attempt at catheterization, a mass measuring approximately 2 × 2 × 1 cm. was seen to occupy the posterior portion of the vulva. This mass appeared to encroach upon the urethra. It was of cystic consistency, and almost doubled in size when intra-abdominal pressure was increased with crying effort. Regression to the original size was observed when the baby became quiet. No hymenal orifice was present.

The child was catheterized, and several hundred cubic centimeters of urine were withdrawn. The catheter traversed the urethra with some difficulty, indicating that the retention was due to the vulval cyst. After catheterization, abdominal palpation revealed a large mass in the abdomen, the superior margin being 2 cm. above the umbilicus. Laterally, the mass could be palpated completely across the abdomen.

A flat abdominal film showed a slight increase in density in the right lower quadrant (Fig. 1)—too indefinite a finding to warrant a diagnosis of a pathological entity. Recatheterization and injection of diodrast showed the bladder to be distended, forced to the right and anteriorly (Figs. 2 and 3). The bladder was emptied and the cystic mass in the vulva punctured with an intravenous needle. A syringeful of white mucoid substance, about the consistency of egg white, was withdrawn. Much more of this material was present, but was left *in situ* temporarily. Culture proved it to be sterile, and microscopic examination disclosed many desquamated epithelial cells. Twenty cubic centimeters of diodrast were then injected into the cyst.

Anteroposterior and lateral films revealed a massive, cone-shaped cavity, 8 cm. long, with its apex directed downward, and in direct continuity with what was apparently the lower portion of the infant's vagina (Figs. 4 and 5). It was clear from the roentgenogram that the small oval structure in the vulva was in direct continuity with the larger one in the peritoneal cavity (Fig. 5). The exact relationship of the bladder to these structures was determined by a lateral film (Fig. 6). The bladder and cystic structure were clearly outlined. Pressure on the neck of the bladder was obvious. The "cyst" was a tremendously dilated uterus and vagina, caused by the damming up of secreted mucoid material from the cervix and uterus.

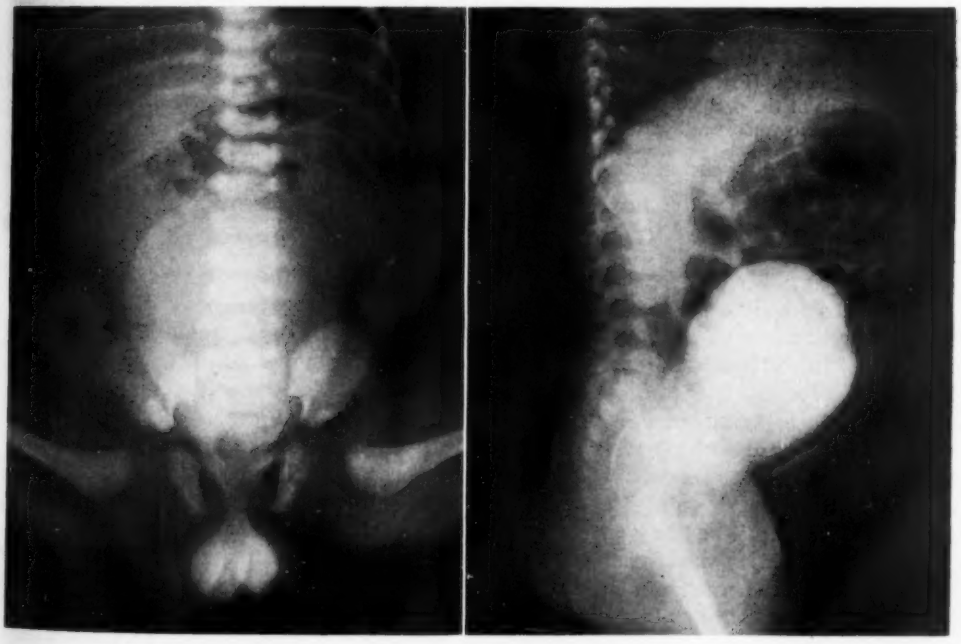
Fig. 1. Flat plate of abdomen, showing a slight increase in density, predominantly on the right side.

The membrane thought to be the hymen was incised, and the redundant tissue tacked to the vulva with a few sutures. Approximately 400 c.c. of the contained mucoid material previously described gushed forth, and simultaneously the infant voided a large quantity of urine. Since the so-called "hymen" proved to be at least 2 mm. thick when incised, it was considered that an atresia of the lowermost vagina had probably existed.

The infant's urinary difficulties ceased; the

[1] From the Radiology Department, Rochester General Hospital, Rochester, N. Y. John W. MacCauley Prize Essay presented at the Annual Meeting of the Rochester Academy of Medicine, May 6, 1947. Accepted for publication in October 1947.

Figs. 2 and 3. Roentgenograms obtained after catheterization and injection of diodrast. Fig. 2 (left) shows the bladder to be distended and forced completely to the right. Fig. 3 (right), the lateral view, illustrates the concavity of the posterior portion of the bladder, giving the impression of a mass behind it.



Figs. 4 and 5. Views obtained after injection of diodrast into the cystic mass in the vulva. Fig. 4 (left) shows the entire genital tract of the infant massively dilated. The smaller cystic mass protruding between the labia is in direct continuity with the larger mass in the abdomen. Diodrast previously withdrawn from bladder. Fig. 5 (right) is a lateral view of the large cystic mass. A small amount of diodrast still clings to the walls of the bladder.

Fig. 6. The cystic mass and the bladder are shown in relation to each other by diodrast injection into both.

masses, both abdominal and vulval, disappeared; and a roentgenogram obtained seven months later showed the uterus, although still enlarged, to be much reduced in size (Fig. 7).

The diagnosis of the pathological entity apparent from the roentgenograms, was hydrometrocolpos.

A few cases of hydrometrocolpos have been reported in the literature to date. Ladd and Gross (1) give a short discussion of the condition, and hypothesize upon the possible origin, although most of their material comes from the best article on the subject, written by Mahoney and Chamberlain (2), who reported 3 cases. Rosenblatt and Woolley successfully treated 1 case (3). A single instance of this condition could be found in the British literature, namely Spencer's (4) report in 1916. Kereszturi, however, found 7 cases in the foreign literature, the first having been published in 1856 by the French physician, Godefoy; 3 more came from the French, 2 from the German, and 1 from the Italian literature. Five of these patients were two months of age, or less; 2 were six and seven years old, respectively. In all there was an imperforate hymen. Three suffered acute urinary retention All underwent hymenectomy, with release of fluid—from a few cubic centimeters to 300 c.c. Its character varied from fetid pus to thin mucus. To these cases Kereszturi (5) added a case of her own in a six-weeks-old child who became anuric after having had urinary distress since birth. Intravenous pyelograms revealed bilateral hydronephrosis with obstruction at the uterovesical junction. An imperforate hymen was dismissed as having nothing to do with the condition. Laparotomy revealed a large pelvic tumor which caused a bulging of the hymen when pressed upon. The hymen was incised and 2 ounces of milky fluid were released, with a collapse of the intra-abdominal mass. At twenty-two months of age, an intravenous urogram showed the condition to have regressed, and the patient remained symptom-free.

Morris (6) reported a case of hydrometrocolpos as a cause of "urinary retention, intestinal obstruction, and edema of the lower extremities" in an infant seven weeks of age. Unfortunately, this patient was submitted to laparotomy before the true nature of the condition was recognized, and expired thirty-four days postoperatively after wound disruption and formation of a fecal fistula. In addition, Morris refers to 2 interesting cases, one in a 14-year-old girl from whom 2,200 c.c. of blood-free fluid were released after incision of the imperforate hymen, and the other that of a 72-year-old woman with the presenting symptoms of urinary and intestinal obstruction, evidently following a senile vaginitis which resulted in vaginal stenosis.

In the past, when the condition went unrecognized, hydronephrosis and pyelonephritis have occurred, due to the urinary tract obstruction. Intestinal obstruction has not been uncommon. Rarely, the "tumor" has unwittingly been removed by surgical means before it was realized that a hysterectomy was being performed on the patient. Mahoney and Chamberlain seem to think that it is not an imperforate hymen that most of these patients have, but rather an atresia of the lower vagina itself.

In a case coming to autopsy they found that the closure was definitely above the usual level of the hymen.

Regarding the origin of the large amount of fluid in our case, one might postulate that it originated from the fetal cervix, under the influence of estrogen stimulation from the mother, *in utero*. Since the exit for the secretion was closed off, due to the obstruction of the vaginal outlet, dilatation of the genital tract resulted. It has been shown by Dobszay (7) that injection of large amounts of estrogen into older infants results in the development of an adult type of vaginal mucosa—precisely the type one finds in a normal newborn child. This of course rapidly regresses once the infant is away from the hormonal influence of the mother. Thus the newborn child has normally a more adult genital tract than the infant six months of age. In fact, the newborn child at times shows a slight amount of vaginal bleeding about the third day after delivery, and hypertrophy of the uterus of the newborn has been demonstrable postmortem. It is also demonstrable that this hypertrophy ceases and a rapid involution to the normal infantile genital state usually takes place within a few weeks after birth. Another indication of maternal hormonal influence upon the child is the readily palpable increase in size of some infant breasts during the first few weeks of life. This enlargement has been proved to be due to estrogen stimulation (8). There can be no doubt that maternal estrogens can and do have an effect on the newborn.

In the case here recorded, hyperestrogenism and perhaps a granulosa-cell tumor were hypothesized as a cause for possible high estrogen levels in the mother, resulting in the tremendous cervical secretion in the child. The problem was investigated after the biological method of Hartman and Littrell (9) for the determination of exact quantities of total estrogen in the human. They have recently been able to detect the presence of less than five one-millionths of a milligram of total estrogen per cubic centimeter of blood by their method. The test is apparently reliable,

Fig. 7. The uterus, seven months after treatment.

since males have invariably given negative results, while almost 100 per cent of females in the intermenstrual period have been positive.

The test depends upon the fact that in young, immature rats (sixteen to twenty-three days old) the closed vaginal vault will open in four to five days or earlier under the influence of 0.02 c.c. of intermenstrual blood. Therefore, by graduated dilution of the mother's blood, any gross increase in her estrogen titer could be determined.

The test was carried out on both mother and infant. The father's blood and sterile saline were used as controls. Ten female rats were used. None of the rats showed any change at the end of ten days, and the test was regarded as negative. Evidently the theory of a high estrogen titer could not hold ground here. The fact that the child did not have enlarged breasts after birth, is further evidence that the mother probably remained within the wide variance of normal for estrogen titers during pregnancy. It might, however, be worth while to repeat the test in a future case, since it was performed here six weeks after

delivery. It might possibly have been significant had it been done earlier.

The exact cause, then, for the copious cervical and uterine secretions still remains a mystery.

SUMMARY

A case of hydrometrocolpos in a newborn infant is recorded.

Since urinary and intestinal difficulties soon develop in untreated cases, early diagnosis is important. This is a simple matter with the aid of a contrast medium, such as diodrast.

Simple incision with creation of a vaginal outlet results in release of the dammed back fluid, and rapid involution of the distended uterus and vagina.

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SUMARIO

Hidrometrocolpos Congénito. Comunicación de un Caso

Preséntase un caso de hidrometrocolpos en una recién nacida.

Visto que en los casos no tratados pronto se manifiestan trastornos urinarios e intestinales, el diagnóstico temprano resulta importante. Esto es fácil con la ayuda de un medio de contraste, como el diodrasto.

La incisión simple con la creación de una salida vaginal logra la expulsión del líquido retenido y la rápida involución de los distendidos útero y vagina.

Calcification of the Ascending Aorta as a Sign of Syphilitic Aortitis[1]

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IN 1945 JACKMAN and Lubert (1) reported that they had noted a frequent association between syphilitic aortitis and calcification of the ascending aorta. Their series of cases appeared to demonstrate that, while calcification of the ascending aorta appears on routine roentgenograms of the chest in only about 25 per cent of the cases of syphilitic aortitis, it is a valuable diagnostic sign when present. The only previous mention of this finding which they (or the present writer) were able to find in the literature were the casual statements of Snellen (3) and Schatzki (4). These authors merely reported figures and impressions and made no effort at statistical analysis.

The article of Jackman and Lubert led the present writer to investigate the serology and clinical cardiac findings in several cases showing calcification in the ascending aorta on routine admission chest roentgenograms. These patients were found to have positive Wassermann reactions and in one case a definite aortic insufficiency. The suggestion of syphilitic aortitis on the basis of this sign was skeptically received and consequently the present study was undertaken.

The material is divided into three groups. Group I consists of all of the cases of syphilitic aortitis, proved at autopsy, which could be found locally, in which chest roentgenograms were available. Group II consists of all cases of clinically diagnosed syphilitis aortitis with chest roentgenograms. Group III is made up of consecutive cases in which calcification of the ascending aorta was demonstrated on routine chest examination. Pertinent information on each patient was carefully tabulated. The individual case data are omitted because of space limitations.

ANALYSIS OF FINDINGS

For the purposes of control, 400 roentgenograms of the chest were examined. These were consecutive cases drawn from a routine file, unselected except for age and sex. Distribution by age and sex was made to correspond to that of the combined clinical and autopsy groups in which syphilis was present. Calcification of the ascending aorta was found in 2 cases in this control group, an incidence of 0.5 per cent.

Twenty autopsy protocols of cases with a definite diagnosis of syphilitic aortitis and with chest roentgenograms were available. Of these, 11 showed calcification of the type under consideration. In 2 of the 11, aneurysm was present. Two other cases showed aneurysm without calcification. Therefore, 9 of 18 cases, or 50 per cent of cases of aortitis without aneurysm, proved at autopsy, showed calcification in the ascending aorta.

There were 39 cases in which the diagnosis of syphilitic aortitis had been made at the University Hospital or the Minneapolis General Hospital. Of these, 21 showed the calcification in question. Four of the 21 were felt to have aneurysms of the aorta. Omitting these, 17 cases, or 43 per cent of the total number, showed calcification. Of the total number 66 per cent had positive Wassermann reactions.

During the period of the study 21 cases of calcification of the ascending aorta were found on routine postero-anterior

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[2] Trainee of the National Cancer Institute.

TABLE I: CALCIFICATION OF THE ASCENDING AORTA IN SYPHILITIC AORTITIS: COMPARISON OF AUTHOR'S SERIES WITH THAT OF JACKMAN AND LUBERT (1)

	Serology Positive	Calcification of Ascending Aorta
Autopsy Cases		
Present Series	80% (16 of 20)	50% (9 of 18)
Jackman and Lubert	80% (49 of 61)	22.7% (15 of 51)
Clinical Cases		
Present Series	65% (26 of 39)	41% (16 of 39)
Cases Showing Calcification on Routine Chest Examination		Clinical Evidence of Aortitis
Present Series	62% (13 of 21)	30–90%* (12 of 13)
Jackman and Lubert	65% (13 of 20)	25% (5 of 20)

* The range of percentages depends upon whether the clinical criteria were felt to be conclusive (low figure) or included those merely suggestive (high figure).

films of the chest; 13 of these, or 62 per cent, were associated with a positive Wassermann reaction, demonstrating a definite relationship between the calcification and syphilitic infection. Four of the 13, or 30 per cent, had other findings warranting a clinical diagnosis of syphilitic aortitis; 1 was not well worked up from a cardiac standpoint. Seven others showed a high pulse pressure but no other clinical signs of aortitis; 1 had tabes dorsalis and 3 had psychoses of unclassified type. In one of the latter a presumptive diagnosis of syphilitic aortitis was made. Thus, there was definite evidence of syphilitic aortitis in 4 cases and suggestive evidence favoring this diagnosis in 8 cases, a total of 12 cases out of 13, or 92 per cent. Thus a positive serologic test, plus calcification in the ascending aorta in the same patient, indicates that syphilitic aortitis is probably present.

Table I shows a comparison of percentages in our group and in that reported by Jackman and Lubert. That the figures in the two series are in agreement within the variations imposed by the small numbers of cases is apparent. Percentages are given because they are more convenient to compare; the large inherent error is recognized. There appears to be no question that the conclusions drawn are statistically warranted.

Jackman and Lubert give an excellent review of the literature and bibliography. The reader is referred to their article (1) for this material.

CONCLUSIONS

1. The presence of calcification in the ascending aorta is a valuable diagnostic sign of syphilitic aortitis but absence of such calcification is of no significance.
2. Calcification in the ascending aorta occurs chiefly in elderly individuals.
3. The contentions of Jackman and Lubert are confirmed.

NOTE: The author is deeply grateful to Dr. B. J. Clawson of the Pathology Department of the University of Minnesota for making autopsy material available and to numerous others who helped in the collection of cases for routine chest examination.

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SUMARIO

La Calcificación de la Aorta Ascendente como Signo de Aortitis Sifilítica

Considérase la presencia de calcificación en la aorta ascendente como valioso signo diacrítico de aortitis sifilítica, aunque la falta de dicha calcificación carece de importancia diagnóstica.

El signo se hallaba presente en 9 (50 por ciento) de 18 casos de aortitis sifilítica sin aneurisma y en 16 (41 por ciento) de 39 casos con diagnóstico clínico de aortitis sifilítica. La incidencia en un grupo testigo compuesto de 400 radiografías de enfermos de distribución comparable por edad y sexo, representó 0.5 por ciento.

La asociación entre la calcificación de la aorta ascendente y la aortitis sifilítica fué corroborada por el repaso de un grupo de 21 casos de dicha calcificación. En 13 de estos casos obtúvose una serorreacción positiva para sífilis, y 12 de los 13 mostraban signos clínicos (terminantes o indicativos) de aortitis sifilítica.

Hydronephrosis Causing Displacement of the Splenic Flexure[1]

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DEPRESSION OF THE splenic flexure is usually caused by splenomegaly and can be demonstrated by barium enema. It is unusual for a retroperitoneal structure, such as the kidney, to cause any significant deflection of the bowel. In the case to be presented, the splenic flexure was depressed by a huge hydronephrotic kidney.

of the abdomen, extending to the mid-line and reaching down below the iliac crest. It was firm, nontender, and not ballotable. It was thought to be an enlarged spleen and that impression was strengthened when it was learned that the patient had been under observation for anemia in a large civilian hospital twenty years before. A splenic puncture had been planned at that time but he had left the hospital against advice before it could be performed. The remainder of the past history was essentially

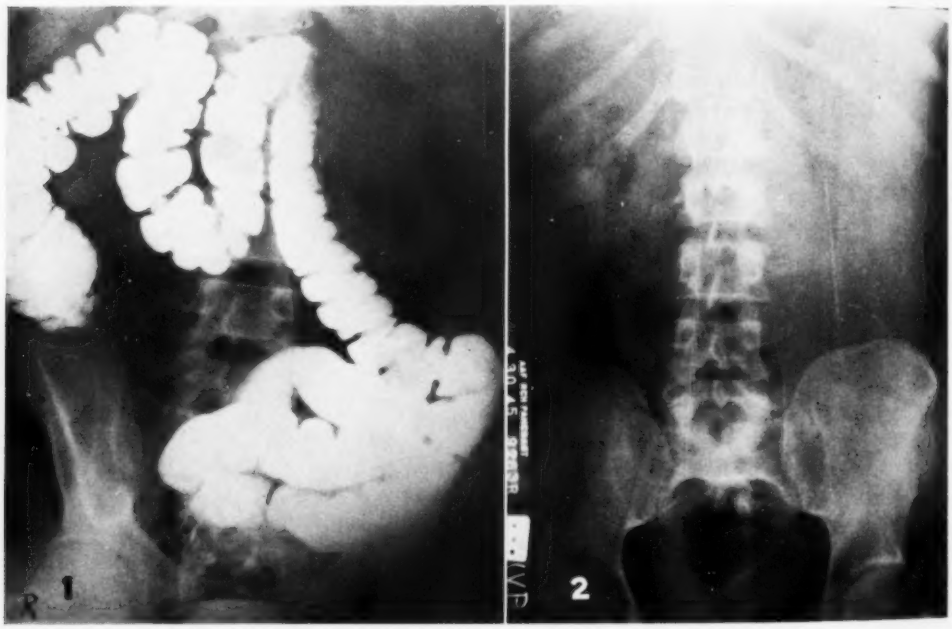

Fig. 1. Barium enema study, showing depression of the splenic flexure.
Fig. 2. Intravenous pyelogram, at fifteen minutes, showing filling of right renal pelvis and non-filling on the left. The outline of the mass as seen on the scout film is also apparent.

S. F., a 37-year-old Negro, was admitted to the AAF Regional and Convalescent Hospital No. 1, Miami Beach, Fla., in April 1945, for physical evaluation following two and half years service in India and China. He complained of tiring easily, and a blood count disclosed a secondary anemia (red cells 3,100,000; hemoglobin 9.2 gm.) of the normocytic type. Physical examination was essentially negative except for a huge mass, which filled the left upper quadrant

negative. The patient denied having had malaria but had suffered several attacks of dysentery while in Asia.

A scout film showed a large, dense mass filling the left side of the abdomen, corresponding to the finding on physical examination. On a barium enema study the stream of barium was seen, fluoroscopically, to swirl up, then downward and across the abdomen around the tumor. A film (Fig. 1) showed

[1] Accepted for publication in October 1947.
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marked depression of the splenic flexure, confirming the fluoroscopic findings. While these observations were consistent with an enlarged spleen, enlargement of so great a degree for a period of twenty years, without further evidence of disease, was regarded as unusual, and the possibility of some other explanation for the mass was considered. Accordingly excretory urography was undertaken, disclosing normal filling of the urinary tract on the right side but no filling on the left (Fig. 2). An attempt to do a retrograde study was unsuccessful.

A working diagnosis of left hydronephrosis was made and the mass was exposed through the usual left loin incision. It was impossible to deliver the tremendous bag of water into the wound and 4,600 c.c. was suctioned off before the hydronephrotic sac was removed. Convalescence was uneventful and the patient was later discharged to duty.

SUMMARY

A case is reported in which a huge hydronephrotic kidney produced marked depression of the splenic flexure. This type of displacement by a retroperitoneal structure such as the kidney is believed to be unusual.

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SUMARIO

Hidronefrosis como Causa de Desplazamiento de la Flexura Esplénica

Comunícase un caso en el cual un enorme riñón hidronefrótico produjo hundimiento pronunciado de la flexura esplénica. Considérase rara esta forma de desplazamiento ocasionada por un órgano retroperitoneal como es el riñón.

EDITORIAL

Teaching Physics to Medical Students

At the Annual Conference of Teachers of Clinical Radiology[1] sponsored by the College of Radiology, a symposium on the teaching of physics was presented, a summary of which will be published elsewhere.[2]

The need of a knowledge of physics has recently become more acute and more obvious. The medical profession is swarming into the field of nuclear energy opened by the physicists. The latter have been extremely co-operative, but that is not enough. The doctors must now learn physics. The situation is something like that incident to the development of biochemistry as a branch of medicine, but greatly telescoped. Radioisotopes are available in adequate quantities and we must hurry to learn to use them. For therapy, only P^{32} and I^{131} have proved themselves so far, but the field of tracer technics (diagnosis and research) is wide open. Dr. Andrew Dowdy quoted from a report that he and Dr. Stafford Warren prepared for the American Medical Association, the following objectives:

"1. So to train our medical scientists that they will be capable of competition, medically, socially and as world citizens, in the age of nuclear energy.

"2. Basic training in the bio-physical approach to current medical problems, with special emphasis on nuclear energy.

"3. Postgraduate training of individuals in the highly specialized fields of radiology, biophysics, industrial medicine, and health physics.

"4. To build a reserve pool of scientifically trained personnel whose special talents may be utilized in the case of a national emergency.

"5. In some instances, to facilitate the training of personnel from the armed services."

[1] Chicago, Ill., Feb. 8 1948.

[2] Proceedings of American College of Radiology (Commission on Education).

He concluded that future medical students would have to have a broad basic training in the fundamentals of atomic structure, nuclear structure, radioactivity, and isotope technic. They must know something of chemical *versus* radiation toxicity of various unusual materials, particularly those that are used in the pile. They must become acquainted with Geiger counters, mass spectrographs, electron microscopes, ultraviolet and infra-red spectroscopy, etc.

"This means there is going to have to be some alteration of our medical school curriculum. It even starts in our elementary schools. The present low salaries paid to elementary school and college teachers are not conducive to the best development of the young minds. If the trend continues (salaries so low as to fail to attract able teachers into elementary schools and colleges) we will be receiving medical students who are mentally emasculated."

The teaching of physics ought to start early and there is no sense in delaying the introduction of atomic physics. It need not be more difficult—and can easily be more exciting—than mechanics.

There was a difference of opinion among the participants in the Symposium as to whether premedical students ought to take a course in engineering physics and study mathematics through calculus. Dr. George Henny and Dr. Howard Hunt and Mr. Herbert Parker thought they should, but Dr. M. L. Pool and Dr. Dowdy thought that they and the arts college students should have their physics explained in simple terms avoiding higher mathematics. It takes good teachers to do that. It is fine, of course, to have a mathematical mind, but can we say that only a person with that kind of a mind can become a really good

doctor? Dr. Brues was sure that medical students were not going to catch up with the mathematics required in isotope work. They'll head into it unprepared and have to learn whatever practical mathematics they need at the time they need it.

Dr. Pool wanted to see physics classes broken into small sections, each taught by one man who would give lectures, quizzes, laboratory work, and examinations. He thought it a mistake to cling to textbooks and laboratory manuals and to try to cover everything. If the student is taught fewer things, and so taught that he really understands them, he will gain confidence that he will be able to understand other things when he inevitably meets them. There is no disadvantage, then, but only advantage, in the fact that the several sections will be taught different things according to the enthusiasms of the different teachers.

Dr. Dowdy felt that the whole structure of medical education had been kept too rigid, courses being merely tacked on under the impulse of rapid scientific advances in many fields. Dr. Henny quoted J. J. Thomson: "It is not enough borne in mind that the capacities of pupils do not stretch proportionately with the increase in knowledge, and that if new matter is to be included, some old matter must be jettisoned to make room for it."

Dr. Leo Rigler found the older scientists unwilling to give up any hours for the newer things. He spoke of students spending some thirty-seven hours a week actually being talked at or working in the laboratory or clinic, and so having desperately little time for thinking. He believed we ought to dig six weeks out of the summer vacation. Students are today using their vacations to earn money—at a dollar an hour—instead of working at their careers (studying medicine) and hastening the time when they can earn ten times as much. These are grown men. Men don't cultivate their careers a short eight months in the year. But the faculty must not be made to teach fifty weeks in the year, for they will become tired out and all the fire be gone from their teaching.

Dr. Dowdy proposed quite definitely to make nuclear energy a required eighteen-hour course for first-year medical students. He would expect their special knowledge to be enlarged by incidental teaching in courses in biochemistry, pharmacology, physiology, medicine, etc. Professors of radiology could deepen their understanding in this field. The didactic course would come at a time when the "memory courses" (anatomy, histology) would leave more free the mental energy needed to attain understanding in the field of nuclear physics.

Mr. Parker gave a definition of Health Physics: "a borderline subject surrounded by industrial medicine, radio-biology, industrial safety, public health, industrial hygiene, physics, engineering, and chemistry. The area between these boundaries is ill-defined." He thought suitable extensions from the boundaries might, in a proper medical school, cover the region so well that no "health physics" would be left. At least he would not put such a course into the curriculum. He did think that current education shows a woeful lack of indoctrination in safety in all laboratories and that a natural place to teach the safe handling of the tools of a trade is in the place where they are being used, not in a didactic course. He believed that present training of radiologists in dosimetry is generally inadequate, and remarked that, for a health physicist, fifty hours each of class and laboratory is needed in this field. When asked if doctors weren't going to have to measure radiation in case of atomic bombing, he replied that their services would be much more critically required in aiding the people already injured.

Dr. Henny urged a course in medical physics—"biophysics" he would prefer to call it—and cited some published sources of medical examples illustrating various physical principles.[3] Such a course, he believed, could be made extremely interest-

[3] BOCKSTAHLER *et al.*: Am. J. Physics **14:** 338, 1946. Also STRAIT *et al.*: Am. J. Physics **15**. 375, 1947. LOOFBOUROW: Rev. Mod. Physics **12**: 267, 1940.

ing but should not be taught at a low intellectual level. He quoted Chamberlain: "No student, except he be a physics major, needs physics to a greater degree than the prospective physician, for no other subject can compete with physics in the development of those habits of exact thinking and inquiring self-criticism which are important to the modern physician."

Physics requirements will fall most heavily on those who desire to specialize in radiology. Dr. Dowdy remarked that it is already four or five years from graduation to specialty board, and that the year of internship seems indispensable. It seems impossible to put much more course work into the three years of residency training. While some improvement in seminars and in departmental organization is obviously possible, for those who expect to be active in the new field of isotopes yet another year will probably be required. This should supplement the three years' training in clinical radiology, not precede it. Too few schools are equipped in activities or personnel to give such training. A policy of exchanging residents was suggested, leaving each school free to develop and improve some particular feature of the needed training. Another possibility is a year of residence in an affiliated national laboratory. Such residencies or fellowships are already being arranged at Oak Ridge (University of Tennessee) and Argonne (University of Chicago).

Dr. Fred Jenner Hodges remarked their good fortune at Michigan in having already a research institute and a shop in connection with the Radiology Department, and having early acquired some knowledge and experience in the isotopes field. He realized that tracer studies are removed from the field in which clinical radiologists ordinarily work. Although radiologists might feel that anything belonging to radiant energy must fall in their specialty, only future experience can tell whether radiology ought to be expanded to include this new responsibility. At any rate, radiology, as a medical specialty, would be remiss if it did not seek to inform itself broadly and thoroughly in the new field, if only to counsel its colleagues regarding the precautions which radiology has found to be imperative through many bitter lessons learned during its own past. For the moment, departments of radiology should seek to control the handling, assaying, dispensing, and ultimately the disposal of radioactive material. "In carrying out these self-assumed obligations," said Dr. Hodges, "it may well transpire that isotope medicine will become a permanent protectorate of radiology." Radiologists, however, will do well not to take this for granted. In their relation to other doctors who are using radioisotopes they will have to make sure that they act in a spirit of helpfulness, not of jealousy.

R. R. NEWELL, M.D.

The Registry of Radiological Pathology

The first appointment to the Fellowship in Radiological Pathology sponsored by the Radiological Society of North America has been confirmed by the Director of the Army Institute of Pathology, Washington, D. C. His study will be in the Registry of Radiological Pathology, a newly established branch of the American Registry of Pathology.[1]

The American Registry of Pathology was established in 1922 under the auspices of the National Research Council and contains registries of special pathology in the fields of ophthalmology, otolaryngology, urology, orthopedics, and thoracic surgery, the aim of which is to collect cases of proved pathologic conditions, study the gross and microscopic material, clinical histories, laboratory and radiological data, clinical course and prognosis, and then arrange these findings in some suitable form so

[1] See announcement, p. 268.

that they can be loaned to physicians for study.

The establishment of a Registry of Radiological Pathology and the correlated fellowship should make many valuable contributions to the science of radiology. Historically, it represents a commendable example of co-ordinated activity of our three societies, the American Roentgen Ray Society, the Radiological Society of North America, and the American College of Radiology. The latter group has appropriated $2,500 for the annual expenses of the Registry and each of the other societies is supporting two six-month fellowship appointments annually. The government contribution to this program will be even greater. Not only will the newly created Registry of Radiological Pathology have the use of a share of the professional, technical, and clerical services of the Army Institute of Pathology, but the expenses of consultant services will be met from government funds.

Upon the skill and energy of these consultants will depend much of the success of the project. There are many important questions to be decided in the first years of the study. How is it to co-ordinate with the already established registries? In the fields of chest and bone tumors, for example, there is much radiological material already available for review; newly acquired cases from radiologists should be available for classification in these registries. Decisions must be reached as to the form in which cases will be made available for study: film strip, albums, transparencies, and prints all must be evaluated. The selection of cases for inclusion in the study would also rest with these consultants.

Plans for gathering more material from radiologists everywhere will need to be well worked out. There is a tremendous potential never before available for augmenting teaching material if individual radiologists throughout the country, unconnected with teaching centers, can be stimulated to submit their proved cases. Good opportunities may be afforded to evaluate the usefulness of special procedures such as laminagraphy, angiography, and kymography.

The leaders of our societies have clearly stated that in establishing these fellowships they have not committed the societies to an indefinitely continuing future expense. The project must prove its worth not only to teaching hospitals in medical centers but to practising radiologists in every community. This can be done, but it will require vision and energy on the part of the leaders and hard work by those in the fellowship positions.

GEORGE L. SACKETT, M.D.

ANNOUNCEMENT

American Board of Radiology

The fall examination of the American Board of Radiology will be held at the Hotel Floridan, Tampa, Fla., Nov. 1–5, 1948. The Southern Medical Association is holding its annual meeting in Miami, Oct. 25–28, and the annual Cancer Seminar of the Southeastern States will be held in Tampa, Nov. 8–10. This seminar is sponsored by the American Cancer Society, Florida Division, and the Florida State Board of Health. A large attendance of physicians is expected. It is hoped that as many candidates as possible can attend both of these meetings. All those hoping to be examined in Tampa should have their applications on file with the Secretary not later than Sept. 1, 1948.

B. R. KIRKLIN, M.D., *Secretary*

Lewis G. Allen, M.D.

1891–1948

Radiology has suffered a great loss in the death of Lewis G. Allen, M.D., from acute leukemia, on May 28, 1948, in Providence Hospital, Kansas City, Kan. He is survived by his wife, Pauline McLaughlin Allen, and his two sons, Dr. Lewis G. Allen, Jr., and Dr. William R. Allen.

Born in Lenexa, Kan., on Oct. 19, 1891, and educated at the University of Kansas, Lewis Allen lived out his distinguished career in the State of his birth. He served his internship in the Royal Victoria Hospital, Montreal, in 1917 and immediately entered the military service of his country. He

served overseas as a radiologist and, on his return to civil life, entered the private practice of radiology in Kansas City, Kan. In 1920, he became radiologist to Providence Hospital, and continued in that position until his death. He was also radiologist to Bethany and to St. Margaret's hospitals.

Although he was an active worker in his special field of Radiology, Dr. Allen retained that broad interest in medicine as a whole which characterizes every good worker in a special field. He was a past-president of his County Medical Society and of the Southwest Clinical Society and served on the Council of the Kansas Medical Society. He was also active in the civic life of his community, and, at the time of his death, was a trustee of Group Hospital Service, Inc.; trustee of Boylan Research Fund; and trustee of Wyandotte County Tuberculosis Association.

Dr. Allen made extensive contributions to the medical literature, and maintained an active interest in teaching. For the past ten years he held the rank of Clinical Professor of Roentgenology in the University of Kansas. He was a member of the Radiological Society of North America, the American Radium Society, and the American Roentgen Ray Society, and was a Fellow of the American College of Radiology. He was president of the Radiological Society of North America in 1945, and at the time of his death was a Chancellor of the American College of Radiology.

For all of these contributions to our profession Lewis Allen will be long remembered. Even more will he be remembered for his kindly and gentle spirit and his loyal and unswerving friendship *Requiescat in pace!*

LOWELL S. GOIN, M.D.

Thomas Raymond Healy, M.D.

1879–1948

Dr. Thomas Raymond Healy, for more than twenty-five years a member of the Radiological Society of North America, died on Feb. 25, 1948.

Dr. Healy was a native of Newburyport, Mass. He was graduated from Dartmouth College in 1899, and was licensed to practise the same year. Since 1900, he had been a member of the staff of the Anna Jaques Hospital, Newburyport, first as surgeon and then as radiologist. During his active medical career, he had connections with several greater Boston hospitals, including the Marine Hospital and St. Elizabeth's Hospital.

Dr. Healy served in two world wars. In World War I, he was Chief of the Radiological Department of the U. S. Marines. In 1918, he headed the X-ray Department of the Navy in France, and was later in charge of the same service at the Chelsea Naval Hospital. In World War II, he was Roentgenologist at the Naval Training Station at Newport, R. I. He was retired as Captain in the Naval Reserve.

Beside his membership in the Radiological Society of North America, Dr. Healy was a member of the American Roentgen Ray Society, the American College of Radiology and the New England Roentgen Ray Society. He was a Past-President of the New England Roentgen Ray Society and of the Essex North Medical Society, a Past-Commander of the Newburyport Post of the American Legion, a member of the Veterans of Foreign Wars, and Past-Vice Commander of the National Naval Order. A keen yachting fan, he was a member of the Corinthian Yacht Club and the American Yacht Club.

ANNOUNCEMENT
FELLOWSHIPS OF THE REGISTRY OF RADIOLOGICAL PATHOLOGY

The Registry of Radiological Pathology has been established through the co-operation and support of the American College of Radiology, the American Roentgen Ray Society, and the Radiological Society of North America. This registry is part of the American Registry of Pathology which, in turn, is one of the four divisions of the Army Institute of Pathology and the only division which operates under the auspices of the National Research Council. The Registry is housed in the same building as the Army Medical Library (formerly known as the Surgeon General's Library).

Fellowships in several other specialties are supported at the Institute of Pathology by organizations sponsoring registries; *e.g.*, the American Academy of Ophthalmology, the American Academy of Orthopedic Surgeons, etc. There are over fifteen specialty registries included in the American Registry of Pathology. In the case of the Registry of Radiological Pathology, the College of Radiology supplies funds to the National Research Council for general expenses. The American Roentgen Ray Society and the Radiological Society of North America each supports two six-month fellowships annually, which carry monthly stipends of $250 per Fellow. The four Fellows thus supported receive appointments starting Jan. 1, April 1, July 1, and Oct. 1, respectively, in order that two Fellows may work together and that continuity of effort may be maintained by a three-month overlap of appointments. The work of the Fellows is supervised and coordinated by civilian consultants chosen by the Director of the Institute of Pathology. The consultants are currently Drs. L. H. Garland, Fred J. Hodges, and Merrill C. Sosman.

Applications are now open for the fellowships. The American Roentgen Ray Society fellowships begin July 1 and Jan. 1 and the Radiological Society fellowships on Oct. 1 and April 1.

In order to facilitate the establishment of the Registry, the American Roentgen Ray Society and the Radiological Society of North America have appointed Fellows who are now working at the Registry. The following outline of their activities to date indicates the nature of the fellowships:

Outline of Facilities and Activities of Fellows at the Registry of Radiological Pathology

I. Schedule for routine daily activities.
   A. Study of the histopathologic slide sets prepared by the American Registry of Pathology. One and a half to two hours is suggested.
      1. There are 36 such sets, two of which cover general pathology while the remainder cover specific subjects.
      2. Supervision by a staff pathologist is made available for the Fellow.
   B. Study of roentgenographic teaching aids already prepared.
   C. Attendance at the three weekly conferences of the professional staff of the Institute. At these conferences both typical and unusual cases are presented. The clinical history, physical and roentgenological findings are presented, the gross specimen is demonstrated, and the histological findings are demonstrated by projection.
   D. Attendance at radiological conferences at various Washington hospitals. These include Walter Reed, Garfield Memorial, and Doctors' Hospitals.
   E. Consultation with members of the Institute staff on cases having roentgenograms.

II. The preparation of roentgenographic material at the Registry for teaching aids.
   A. This activity includes two phases:
      1. The addition to such atlases as have been prepared by previous Fellows. This would be done from current cases as they are added to the Registry as well as from material reviewed by the Fellow through his other activities.
      2. The preparation of material on a subject of the Fellow's own choosing (subject to approval by the Registry Committee). It should be emphasized that this provides an excellent opportunity for the Fellow to investigate a problem in which he may have a personal interest and at the same time fulfill his obligation to the Registry. Facilities for this type of work are excellent.

III. The Fellow is called upon to assist other members of the staff in consultation on radiologic aspects of their problems and investigations. By the same token, the Fellow may avail himself of advice on the pathologic aspects of his studies.

The majority of the cases now on file at the Institute of Pathology do not include roentgenograms of satisfactory quality for adequate correlation of roentgenologic and pathologic findings. This is

largely due to the fact that continuous radiological consultation has not previously been available for the assembly of material. One of the chief obligations of the radiological Fellows is to correct this fault in so far as possible by co-operating with the Institute staff. The completeness of the Registry will depend to a large extent on the co-operation of the radiologists of the United States in sending worth-while, completely documented cases to be included in the file.

The Registry Committees which will act as advisors of the Registry and select candidates for Fellowship are as follows:

For the Radiological Society of North America
Dr. Frederick W. O'Brien, Chairman
Dr. John D. Camp
Dr. Robert S. Stone

For the American Roentgen Ray Society
Dr. Vincent W. Archer, Chairman
Dr. Lyell C. Kinney
Dr. Leo G. Rigler
Dr. Merrill C. Sosman
Dr. Paul C. Swenson

Applications for fellowships may be obtained by writing to the Chairman of either of the above committees. Application should be made to only one committee and will receive due consideration by either or both of the committees. Final approval of all Fellows rests with the Director of the Institute of Pathology.

Details regarding the Registry of Radiological Pathology, its aims, and the steps which led to its establishment may be obtained by writing to Mr. Mac F. Cahal, Secretary, The American College of Radiology, 20 North Wacker Drive, Chicago 6, Ill.

San Francisco, the meeting place of the Radiological Society of North America, Dec. 5–10, 1948. The San Francisco-Oakland Bay Bridge, from the Oakland Side (Union Pacific R. R. Photo).

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer,* Donald S. Childs, M.D., 607 Medical Arts Bldg., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary,* Hugh F. Hare, M.D., 605 Commonwealth Ave., Boston 15, Mass.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary,* Harold Dabney Kerr, M.D., Iowa City, Iowa.

AMERICAN COLLEGE OF RADIOLOGY. *Secretary,* Mac F. Cahal, 20 N. Wacker Dr., Chicago 6, Ill.

SECTION ON RADIOLOGY, A. M. A. *Secretary,* U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Courtney S. Stickley, M.D., Bell Bldg., Montgomery. Next meeting with State Medical Association.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary,* Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary,* Sydney F. Thomas, M.D., Palo Alto Clinic, Palo Alto.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary,* Moris Horwitz, M.D., 2009 Wilshire Blvd., Los Angeles 5. Meets second Wednesday of each month at County Society Bldg.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB. *Secretary,* Charles E. Grayson, M.D., Medico-Dental Bldg., Sacramento 14. Meets at dinner last Monday of September, November, January, March, and May.

PACIFIC ROENTGEN SOCIETY. *Secretary,* L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

SAN DIEGO ROENTGEN SOCIETY. *Secretary,* R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

X-RAY STUDY CLUB OF SAN FRANCISCO. *Secretary,* Ivan J. Miller, M.D., 49 Fourth St. Meets monthly on the third Thursday at 7:45 P.M., January to June at Lane Hall, Stanford University Hospital, and July to December at Langley Porter Clinic, University of California Hospital.

Colorado

DENVER RADIOLOGICAL CLUB. *Secretary,* Mark S. Donovan, M.D., 306 Majestic Bldg., Denver 2. Meets third Friday of each month, at the Colorado School of Medicine and Hospitals.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary,* Robert M. Lowman, M.D., Grace-New Haven Hospital, Grace Unit, New Haven. Meetings bimonthly, second Thursday.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary,* Alfred A. J. Den, M.D., 1801 K St., N. W., Washington 6. Meets third Thursday, January, March, May, and October, at 8:00 P.M., in Medical Society Auditorium.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* J. A. Beals, M.D., St. Luke's Hospital, Jacksonville. Meets in April and in November.

Georgia

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Robert Drane, M.D., De Renne Apartments, Savannah. Meets in November and at the annual meeting of State Medical Association.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary,* T. J. Wachowski, M.D., 310 Ellis Ave., Wheaton. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April, at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly as announced.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary,* John H. Gilmore, M.D., 720 N. Michigan Ave., Chicago 11.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer,* J. A. Campbell, M.D., Indiana University Hospitals, Indianapolis 7. Annual meeting in May.

Iowa

IOWA X-RAY CLUB. *Secretary,* Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Anthony F. Rossitto, M.D., Wichita Hospital, Wichita. Meets annually with State Medical Society.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Sydney E. Johnson, M.D., 101 W. Chestnut St., Louisville.

LOUISVILLE RADIOLOGICAL SOCIETY, *Secretary-Treasurer,* Everett L. Pirkey, Louisville General Hospital, Louisville 2. Meets second Friday of each month at Louisville General Hospital.

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday.

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary*, J. Howard Franz, M.D., 1127 St. Paul St., Baltimore 2.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital, Detroit 1. Meetings first Thursday, October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, C. N. Borman, M.D., 802 Medical Arts Bldg., Minneapolis 2. Meets in Spring and Fall.

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, Wm. M. Kitchen, M.D., 1010 Rialto Building, Kansas City, 6, Mo. Meetings last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Edwin C. Ernst, M.D., 100 Beaumont Medical Bldg. Meets on fourth Wednesday, October to May.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Ralph C. Moore, M.D., Nebraska Methodist Hospital, Omaha 3. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, George Levene, M.D., Massachusetts Memorial Hospitals, Boston. Meets monthly on third Friday at Boston Medical Library.

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary-Treasurer*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meetings quarterly in Concord.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Raphael Pomeranz, M.D., 31 Lincoln Park, Newark 2. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark.

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Abraham H. Levy, M.D., 1354 Carroll St., Bklyn. 13. Meets fourth Tuesday of every month, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*. Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary-Treasurer*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meetings in January, May, and October.

LONG ISLAND RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening, October to May, at 8:45 P.M., in Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Wm. Snow, M.D., 941 Park Ave., New York 28.

QUEENS ROENTGEN RAY SOCIETY. *Secretary*, Jacob E. Goldstein, M.D., 88-29 163rd St., Jamaica 3. Meets fourth Monday of each month.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary*, Murray P. George, M.D., 260 Crittenden Blvd., Rochester 7. Meets at Strong Memorial Hospital, third Monday, September through May.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary-Treasurer*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Charles Heilman, M.D., 1338 Second St., N., Fargo.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Carroll Dundon, M.D., 2065 Adelbert Road, Cleveland 6. Next meeting at annual meeting of the State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Paul D. Meyer, M.D., Grant Hospital, Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Seneca Hotel, Columbus.

CINCINNATI RADIOLOGICAL SOCIETY. *Secretary*, Eugene L. Saenger, M.D., 735 Doctors Bldg., Cincinnati 2. Meets last Monday, September to May.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George L. Sackett, M.D., 10515 Carnegie Ave., Cleveland 6. Meetings at 6:30 P.M. on fourth Monday, October to April, inclusive.

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. E. Brown, M.D., 411 Medical Arts Bldg., Tulsa. Meetings three times a year.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Wm. Y. Burton, M.D., 242 Medical Arts Bldg., Portland 5. Meets monthly, on the second Wednesday, at 8:00 P.M., in the library of the University of Oregon Medical School.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, Arthur Finkelstein, M.D., Graduate Hospital, Philadelphia. Meets first Thursday of each month at 8:00 P.M., from October to May in Thomson Hall, College of Physicians, 21 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY. *Secretary-Treasurer*, R. P. Meader, M.D., 4002 Jenkins Arcade, Pittsburgh 22. Meets second Wednesday of each month at 6:30 P.M., October to June.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Maurice D. Frazer, M.D., Lincoln Clinic, Lincoln, Nebr.

South Carolina

SOUTH CAROLINA X-RAY SOCIETY. *Secretary-Treasurer*, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

Tennessee

MEMPHIS ROENTGEN CLUB. Meetings second Tuesday of each month at University Center.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Marsh Frére, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

Texas

DALLAS-FORT WORTH ROENTGEN STUDY CLUB. *Secretary*, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meetings on third Monday of each month in Dallas in the odd months and in Fort Worth in the even months.

HOUSTON X-RAY CLUB. *Secretary*, Curtis H. Burge, M.D., 3020 San Jacinto, Houston 4. Meetings fourth Monday of each month.

TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth 4. Next meeting Jan. 7–8, 1949.

Utah

UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, M. Lowry Allen, M.D., Judge Bldg., Salt Lake City 1. Meets third Wednesday, January, March, May, September, November.

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE. *Secretary*, Henry H. Lerner, M.D. Meets first and third Thursdays, September to June, inclusive, at Salt Lake County General Hospital.

Virginia

VIRGINIA RADIOLOGICAL SOCIETY. *Secretary*, P. B. Parsons, M.D., Norfolk General Hospital, Norfolk 7.

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Homer V. Hartzell, M.D., 310 Stimson Bldg., Seattle 1. Meetings fourth Monday October through May, at College Club, Seattle.

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, A. Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee 2. Meets monthly on second Monday at the University Club.

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY. *Secretary*, S. R. Beatty, M.D., 185 Hazel St., Oshkosh. Two-day meeting in May and one day with State Medical Society, September.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE. Meets first and third Thursdays 4 P.M., September to May, Service Memorial Institute, Madison 6.

Puerto Rico

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA.—*Secretary*, Jesús Rivera Otero, M.D., Box 3524, Santurce, Puerto Rico.

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, E. M. Crawford, M.D., 2100 Marlowe Ave., Montreal 28, Quebec. Meetings in January and June.

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES. *General Secretary*, Origéne Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday each month.

CUBA

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THE HEAD AND NECK

Encephalography with Small Amounts of Air. Kristian Kristiansen and Agvald Vogt. Acta radiol. **28:** 355-366, Aug. 30, 1947.

In the Neurological Department of the Rikshospital, in Oslo, encephalography with a small amount of air, as originally suggested by Laruelle (Presse méd. **39:** 1888, 1931), has been the routine procedure. A study was made to see if the diagnostic results were satisfactory, and it was found that in the majority of cases the ventricular system was insufficiently filled.

At the first attempt, using 9 c.c. of air, only 11 per cent of the 100 patients examined showed a quantity of air in the ventricles sufficient for diagnosis; in 73 per cent filling was incomplete, and in 15 per cent there was no air at all in the ventricular system. A second attempt, with 12 or 15 c.c. of air, in 46 of the 100 patients, added a further 5 cases with suitable filling for diagnostic purposes. Third, fourth, and fifth attempts, using up to 15 c.c. of air, were made in a few patients, with no success.

The authors are now using 15 to 20 c.c. of air in the first attempt, and if the results are not satisfactory, the next encephalography is done under roentgen control and an amount of air is injected which seems necessary to give a satisfactory filling. They believe that the rational procedure is to perform all encephalographies under roentgenoscopy. The radiologist gets a good impression of the ventricular filling after the injection of 20-25 c.c. of air, and later, if desired, 40 to 50 c.c. may be used. The injection is then discontinued. In the authors' experience 40 to 60 c.c. of air is sufficient in most cases. If no air is seen in the ventricles after the insufflation of 40 c.c., it is, as a rule, of no use to make any further attempt.

Two cases are reported in which abnormalities were overlooked because too little air was used.

Encephalography, of course, is not completely devoid of danger for the patient. If the patient is running a risk when subjected to a large encephalography, however, there is also risk in performing a small one. Three cases are recorded which demonstrate this fact.

Clinical Significance of Hyperostosis Frontalis Interna. Norman G. Schneeberg, George Woolhandler, and Rachmiel Levine. J. Clin. Endocrinol. **7:** 624-635, September 1947.

The term hyperostosis frontalis interna refers to a non-inflammatory, frequently symmetrical thickening of the internal table of the frontal bone of the skull. This hyperostosis may or may not extend to adjacent bony areas or the falx cerebri but it does not involve the external skull surface and thus does not increase the external skull dimensions. The radiologic features have been described by Moore (Am. J. Roentgenol. **35:** 30, 1936. Abst. in Radiology **27:** 386, 1936).

In order to determine the incidence of hyperostosis frontalis interna in patients who had once required x-ray examination of the skull as part of their case study, 150 successive unselected skull films previously taken were reviewed. Lateral skull films were also taken of 50 unselected females over thirty years of age who had never required a skull film prior to this study. A positive film had to show hyperostosis regarded as unequivocal by more than one observer. Doubtful films were excluded. Among the first group of 150 films, 4 cases of hyperostosis frontalis interna were discovered, an incidence of 2.7 per cent. Among 50 women who had had no previous skull films, 6 cases were found, an incidence of 12 per cent.

A detailed study was made of two groups of patients: a control group consisting of 50 female patients, thirty years of age and over, whose clinical picture at one time had required a skull x-ray, which had *not* shown hyperostosis, and of 25 patients with hyperostosis interna. In addition, a total of 657 cases of hyperostosis frontalis interna were collected from the literature.

A survey of this material led to the conclusion that no real clinical entity characteristic of hyperostosis frontalis interna exists. The bony thickenings of the internal table of the frontal bone represent a not uncommon incidental finding discovered either by x-ray of the skull or postmortem and are unrelated to the clinical status of the patient. The striking predominance of the condition in females has intrigued all observers.

Amyoplasia Congenita Associated with Hyperostosis Frontalis Interna. R. N. Herson. Brit. M. J. **2:** 491-492, Sept. 27, 1947.

The author was prompted to report this case of amyoplasia congenita associated with hyperostosis frontalis interna because of the absence of references in the literature to the combination of these two conditions.

The patient was a 61-year-old woman. Since birth her lower limbs had been abducted at the hips and flexed at the hips and knees, while her arms had been extended at the elbows and flexed at the wrists. Movements in all joints had been severely limited. She had had headaches behind the eyes and over the frontal region for as long as she could remember, accompanied on occasion by nausea and vomiting. The patient exhibited gross obesity (weight 74 kg.) with a sitting height of 32 inches. She had a large, fat, ruddy face and hair on the chin and upper lip. Abdominal fat sagged down and partially covered the drawn up legs. The breasts were normally developed and the hair on the head and body was of normal female distribution. The skin was greasy and subject to acne, but there were no striae or abnormal pigmentation.

The positive findings on x-ray examination were congenital deformity of the first and second ribs on the right and a short first rib on the left; a bony bridging between the vertebrae; slight scoliosis and fixation of the right transverse process of L5. The bones of the upper limbs were small, with localized periosteal thickening and deformity of the lower end of the right radius. The bones of the lower limbs were small and rarefied and there was bowing of the tibia and fibula.

A film of the pituitary fossa did not show any definite enlargement. Calcification was seen on the floor of the pituitary fossa extending anteriorly and there was some erosion of the base posteriorly. Lateral films of the skull confirmed the diagnosis of hyperostosis frontalis interna with hyperostosis on the internal surface of the frontal bone without involvement of the outer table, large frontal sinuses, and over-pneumatization of the mastoid cells.

An interesting photograph of the patient is shown.

EDSEL S. REED, M.D.

Sturge-Weber Disease: Clinico-radiologic Picture. Giuseppe Muscettola. Radiol med. (Milan) **33:** 534–550, October 1947.

Sturge-Weber disease is a rare clinical entity which consists of a congenital facial cutaneous hemangioma accompanied by contralateral epileptoid convulsions, exophthalmos, glaucoma, and alterations of the fundus.

Radiologically the skull shows intracranial calcifications on the same side as the cutaneous angioma, and these calcifications may at times show the double contour of calcified angiomatous vessels. With encephalography these patients show a scanty filling of the ventricular system or a filling defect caused by a cerebral hemangioma. In two cases, these cerebral angiomata were demonstrated by arteriography.

The author reports two cases of this interesting condition. CESARE GIANTURCO, M.D.

Cleft Palate and the Mechanism of Speech. Michael C. Oldfield. Brit. J. Surg. **35:** 173–179, October 1947.

The main disability of the cleft palate patient is the defect in speech. The operation for repair of the palate and nasopharyngeal valve is the first stage of treatment. The surgeon must supervise the aftercare until normal speech has been attained. The author gives an excellent description of the physiology of the normal speech mechanism. A radiographic method of demonstrating the position of soft palate, lips, and tongue during articulation of speech sounds is described, with excellent reproductions of radiographs. The lips, tongue, and palate are coated with bismuth, and lipiodol is injected along the floor of the nose and on the upper and lower surfaces of the soft palate. Lateral roentgenograms are then made during the articulation of various sounds. MAX CLIMAN, M.D.

Critical Evaluation of Laminagraphy in Carcinoma of the Larynx. Pier Luigi Cova. Radiol. med. (Milan) **33:** 505–533, October 1947.

The author has had the opportunity of studying with plain and laminagraphic films 60 patients with carcinoma of the larynx who were subsequently operated upon. In addition to radiological observation, all these cases had also undergone the usual clinical and laryngoscopic examinations. The conclusion is reached that laminagraphy is a useful complementary method, inasmuch as it allows the surgeon to obtain a better idea of the anatomical extent of the lesion.

CESARE GIANTURCO, M.D.

THE CHEST

Parallactic Fluoroscopy as an Aid in the Bronchoscopic Extraction of Foreign Bodies. Sölve Welin. Acta radiol. **28:** 313–322, Aug. 30, 1947.

The author describes the localization and bronchoscopic extraction of foreign bodies by means of the fluoroscopic parallax. Extraction of the foreign body is performed with the patient in the supine position on an examination table with the x-ray tube beneath. The bronchoscope is introduced into the relevant main bronchus and then, under fluoroscopic control, is directed toward the foreign body. Due regard is paid to the localization of the foreign body in the sagittal plane, this being determined immediately before by roentgenography. On the fluorescent screen it is possible to observe directly whether the forceps is moving straight toward the foreign body or is deflected medially or laterally to it. Next, the x-ray tube is moved to and fro transversely in the horizontal plane, and from the relative displacement on the screen of the images of the foreign body and the forceps it is possible to establish whether or not the forceps are entering the correct bronchus.

The movement of the tube produces an almost stereoscopic impression. If the image of the foreign body should move more than the image of the forceps, the location is dorsal to the latter. Should it move less, it is ventral to the forceps. When the forceps have entered the correct bronchus, both images move equally, and not until then must the endoscopist try to grasp the foreign body. The author has not found it necessary to use biplane fluoroscopy.

Six cases in which this method of foreign body localization was employed are reported.

Mass Radiography of the Chest. A Report. Gísli Fr. Petersen. Acta radiol. **28:** 400–404, Aug. 30, 1947.

During a four-month tuberculosis case-finding program in 1945, 43,595 persons in Reykjavik, Iceland, were examined by tuberculin test, by photofluorography, and by fluoroscopy. Of those expected to be able to report, 98.15 per cent came for examination. Another 522 persons (invalids, aged, and infirm, etc.) were incompletely examined. This leaves only 0.68 per cent of the population who were not examined.

About 31,600 photofluorograms (4 × 5″ films) were obtained. A total of 1,329 persons were re-examined for various reasons. Seventy-one (0.16 per cent) cases of active pulmonary tuberculosis were found; in 56.3 per cent of this number the findings were positive on sputum examination and gastric lavage. The majority of the new cases were in the age group fifteen to thirty.

Compared with full-size films of the same patient, the miniature films proved quite clear and reliable.

Follow-up Procedure on Cases and Suspected Cases Found in Mass X-Ray Survey. Hilbert Mark. J. Kansas M. Soc. **48:** 451–456, October 1947.

The problem presented when abnormal findings are noted in mass survey photofluorographic films is discussed in considerable detail. The large number of etiologic diagnoses that must be considered is listed, and recommendations on the methods of obtaining accurate diagnoses and the team work that is essential between public health officials, radiologists, and clinicians are clearly stated. Further comment on the proper disposition of patients, with respect to public safety and the welfare of the patient is made. The article is based on extensive experience in the state of Minnesota.

ALTON S. HANSEN, M.D.

Erythema Nodosum. Cutting B. Favour and Merrill C. Sosman. Arch. Int. Med. **80:** 435–453, October 1947.

A study was made of patients with erythema nodosum seen at the Peter Bent Brigham and the Children's Hospital (Boston) during the past thirty years. Among 102 adults, 88 were women (86 per cent), and among 53 children twelve years of age or younger, 32 were girls (60 per cent). The age at onset varied from three to sixty-six years. The majority of the patients were between twenty and forty years of age, and 20 were over fifty.

The absence of rheumatic fever and tuberculosis in the detailed family histories is striking. In the group of 155 patients, there were 15 who had a history of chorea or rheumatic heart disease in a parent, sibling, aunt, or uncle. Two of the 15 persons and one other patient in whose family there was no history of rheumatic disease also had a parent or sibling who had erythema nodosum. Three patients gave a history of exposure to active tuberculosis and an additional 10 of exposure to tuberculosis in the household.

A history of recurrent sore throat was common. Attacks of migratory polyarthritis lasting days to weeks, not accompanied by erythema nodosum, occurred one to twenty years before the onset of erythema nodosum in 20 of the adults but in none of the children. A known respiratory infection antedated erythema nodosum in 126 patients (81 per cent). The lag between the infection and the onset of erythema nodosum was usually two to four weeks.

The one constant physical finding was the cutaneous lesion. It began as a firm tender subcutaneous nodule 1 to 2 cm. in diameter. Subsequently, edema and erythema, soon followed by a bruised appearance, developed in the overlying skin. The second most characteristic physical finding was arthritis: 80 adults and 13 children had pains in the joints. Seventy of the 155 patients had palpable cervical adenopathy—part of a recent or present infection of the throat. Nine patients had infections of the lower respiratory tract. In about one-half of the patients for whom cultures were done, beta hemolytic streptococci were grown in material from the throat. Of 61 patients tested with tuberculin, 29 reacted positively. This reflects only the incidence of positive reactors in the population at large in this region. Mild secondary anemia was common.

X-ray examinations of the chest were made of 65 patients during the active stage of the disease. In 37, the findings were entirely normal in all respects. Twenty-eight had pulmonary changes, but in two-thirds of this number the changes were non-specific and not characteristic. There was usually a slight accentuation of the normal pulmonary markings, similar to that seen in acute respiratory infection or in acute bronchitis. Two of this group had fine, diffuse mottling of both lungs resembling that seen in the earliest stages of silicosis. Three others had small areas of localized infiltration; in 2 these were interpreted as areas of pulmonary tuberculosis, obsolete in 1, and in the other (a patient with scrofula) of questionable activity.

Roentgenograms of the painful swollen joints were made for several patients, and in some instances were repeated at later examinations. None showed any abnormality of the joints, and the adjacent bones were entirely normal except for occasional atrophy from disuse. Films of the nasal accessory sinuses showed a high percentage of chronic sinusitis. Since sinusitis alone is common in New England, the roentgen findings are not considered significant.

Well defined Ghon tubercles were rare in the entire group, and only one patient had calcification in the hilar lymph nodes, already present at the time of erythema nodosum.

Erythema nodosum is usually a self-limited disease of one to five weeks duration. Attacks may smolder on in a subacute stage for three to nine months and occasionally for years (5 patients). Removal of the tonsils or any other source of infection is important. One patient in the series seemed to improve immediately after treatment with sulfadiazine. Many others did not respond to sulfonamides, and several patients treated with intensive courses of penicillin did not recover more rapidly than would be expected without specific therapy. Roentgen irradiation of hypertrophied lymphoid tissue in the pharynx lengthened the asymptomatic intervals in chronic relapsing erythema nodosum. In one patient a mild dose of roentgen rays to the mediastinum caused an unexpectedly severe general reaction, and the authors do not advise roentgen treatment even as a diagnostic test.

A follow-up examination one year or longer after the onset of erythema nodosum was made on 61 patients. Five of this group had rheumatic heart disease, but in 4 of these it had been present before the development of the erythema nodosum. Roentgen examinations of the heart and lungs were made a year or more after the acute stage of the disease in 30 patients. None of these patients showed any roentgenographic evidence of pulmonary tuberculosis, and in none of them had calcification developed in the bronchial nodes. The follow-up period ranged from one to twenty-six years and averaged five years.

The enlargement of the lymph nodes persisted from three to twelve months, usually disappearing in five to seven months. The pulmonary changes were more evanescent, usually disappearing in a few weeks, but persisting in one patient for several months. In none of this group were coarse nodular or streaking areas subsequently found in the lungs, such as would be expected in sarcoidosis and as were reported by Kerley (Brit. J. Radiol. **15:** 155, 1942; **16:** 199, 1943. Abst. in Radiology **39:** 748, 1942; **43:** 200, 1944).

The authors regard erythema nodosum as a hypersensitivity disease. Individual predisposition, a variety of infectious and chemical agents, and local trauma contribute to its occurrence. It is not a form of rheumatic fever.

Coccidioidomycosis in New England. Edward R. H. Kurz and Norman W. Loud. New England J. Med. **237:** 610–616, Oct. 23, 1947.

Coccidioidomycosis is rarely found in the eastern United States but due to the marked migration during the war years and following military service, many unusual diseases will appear in various parts of the country.

Four case reports are presented of coccidioidomycosis as observed in New England. In each case a ring-like shadow was demonstrable in the lung. The first patient had a large granulomatous lesion in the nose, with swelling of the upper lip. Biopsy of the lesion showed *Coccidioides immitis*. The skin test was positive. The second patient had a pilonidal sinus and his chest showed a ring-like shadow in the left infraclavicular region. The third patient had a chronic acne of the face and back and the ring-like shadow was in the upper right lung field. The fourth patient was admitted to the hospital for the removal of a pilonidal sinus and films of his chest showed a ring shadow, 1 cm. in diameter, in the upper left chest. All these patients had spent some time in the desert areas of Texas or California during their military careers. It is believed that the infection was contracted there.

These reports show that coccidioidomycosis will be found scattered throughout the country and that the disease should be considered when ring-like shadows are seen in the lungs or unusual skin conditions, especially

granulomatous changes, are found. Biopsy studies of such lesions will usually show the organism, and skin tests should be positive.

The large granulomatous lesion in the first patient of this series was treated with x-ray therapy and showed a favorable response. JOHN B. MCANENY, M.D.

Sensitivity of Skin to Histoplasmin in Differential Diagnosis of Pulmonary Disease. Marshall E. Groover, Jr., in co-operation with Edward A. Cleve, Siegbert Bornstein, Alfred G. Rice, Augustus F. Galloway, and C. P. Macaluso. Arch. Int. Med. **80:** 496–513, October 1947.

In a group of 1,220 soldiers with roentgen evidence of pulmonary tuberculosis at time of discharge, 93.6 per cent were sensitive to tuberculin, 58.6 per cent were sensitive to histoplasmin and 31.1 per cent were sensitive to coccidioidin. Seven patients in the group were strongly sensitive to histoplasmin and gave negative reactions to tuberculin and coccidioidin. The lesions in all 7 were similar, with characteristics of tuberculosis, except for the absence of acid-fast bacilli in the bronchial secretions and of sensitivity to tuberculin.

Efforts to isolate a fungus characteristic of *Histoplasma capsulatum* from bone marrow, sputum, and lymph nodes of patients with a strong sensitivity of the skin were consistently non-productive.

Patients with a strong reaction to histoplasmin usually showed a mild reaction to coccidioidin; those with a strong reaction to coccidioidin usually had a mild reaction to histoplasmin. This cross-sensitivity reaction is also suggested by the geographic distribution of patients with and without sensitivity to histoplasmin.

There was a considerable difference in the geographic distribution of those with strong reactions to histoplasmin as compared to those with mild reactions.

The incidence of pulmonary calcifications was greater in the group sensitive to histoplasmin than in the groups sensitive to coccidioidin or tuberculin.

Of 528 patients for whom a presumptive diagnosis of pulmonary tuberculosis was made by roentgen studies, 117 were found to have acid-fast bacilli in their bronchial secretions or in gastric washings. The diagnosis of tuberculosis was made for 404 patients with only the following evidence of this disease: (*a*) characteristic roentgen evidence of pulmonary pathema and (*b*) sensitivity of the skin to tuberculin. For 7 patients with no sensitivity of the skin to tuberculin, the diagnosis of pulmonary fibrosis, cause undetermined, was made.

The authors conclude that more exacting criteria for the diagnosis of pulmonary tuberculosis should be available than those obtained by roentgenologic studies and tuberculin tests.

Dynamics of Bronchial Cancer. Sabino Di Rienzo. Rev. méd de Córdoba, April 1947. Abst. in Prensa méd. argent. **34:** 1980, Oct. 10, 1947.

This article proposes the theme that bronchopulmonary cancer brings about dynamic alterations of the air passages which precede the anatomical modifications and permit the diagnosis by direct radiography of a neoplasm at a stage sufficiently early for surgical treatment. An obstructive emphysema is observed during expiration in the lobule or lung affected by the neoplasm. On forced expiration there will be seen marked contrast between the normal permeable zone, which expels the major portion of residual air, and other zones in which the expulsion of air is prevented by the valve-like action of the neoplasm.

Bronchography with lipiodol permits recognition of the dynamic signs of early neoplasm: (*a*) the opaque medium proceeds slowly along the main bronchus as if it had not been aspirated by the lobule; (*b*) the main bronchus does not show the normal variations of caliber during respiratory movements, but remains rigid. When the tumor has destroyed half of the lobule, the opaque medium penetrates only the root of the main bronchus but does not go further, as if there actually existed a mechanical obstacle. The absence of such dynamic alteration suggests a benign process.

JAMES T. CASE, M.D.

Lipoid Pneumonia Simulating Bronchogenic Carcinoma. Robert M. Janes. J. Thoracic Surg. **16:** 451–457, October 1947.

The reason for writing this paper was to report two cases of lipoid pneumonia considered preoperatively to be carcinoma of the lung. The roentgenograms show rather atypical lesions in the right upper lobe in both cases. In one case a biopsy only was done after exposing the lung. In the other case a pneumonectomy was performed.

Perhaps the most interesting feature of the report is the fact that neither patient had a very significant history of ingestion or inhalation of oil and, had the history been obtained preoperatively, it would have been considered inconsequential. The author feels there must be an individual susceptibility to the development of lipoid pneumonia, since so many persons use large amounts of oil without ill effect. A short bibliography is appended. HAROLD O. PETERSON, M.D.

Mediastinal Emphysema Following Thoracoscopy. A Case Report. Irwin G. Karron. Am. Rev. Tuberc. **56:** 308–310, October 1947.

A case is reported of extensive mediastinal emphysema which followed thoracoscopy and resection of an adhesive pleural band. The patient had had a therapeutic pneumothorax prior to the operative procedure. The mediastinal emphysema appeared the day following the thoracoscopy and was associated with widespread and severe subcutaneous emphysema involving the chest, back, neck, right arm, upper right thigh, and scrotum. There was only slight dyspnea and there was no cyanosis. The temperature rose to 101.4° and there followed massive intrapleural and extrapleural fluid accumulations and also evidence of some fluid in the mediastinum. These appeared to be hemorrhagic in nature. The patient made an uneventful recovery and the pneumothorax has been maintained successfully, with closure of the original tuberculous cavity.

L. W. PAUL, M.D.

Mediastinal Cysts and Tumors. Martin L. Bradford, Hugh W. Mahon, and John B. Grow. Surg., Gynec. & Obst. **85:** 467–491, October 1947.

A classification of mediastinal tumors, a combination of the classifications proposed by Carlson, Laipply, and Heuer, is presented. It comprises 9 separate headings: congenital cysts, acquired cysts, connective-tissue tumors, neurogenic tumors, primary tumors of the thymus, primary tumors of lymph nodes, primary and secondary sarcomas, primary and secondary carcinomas, and intrathoracic goiters.

Emphasis is placed on the importance of thoracotomy for pathological diagnosis, with extirpation of the mass if it is operable. Evidence is presented to show that such a procedure is safe and rational.

Thirty-five mediastinal cysts and tumors are presented, with 6 additional cases of conditions to be considered in the differential diagnosis. Roentgenograms are reproduced in 18 cases.

Mediastinal Enterocystoma. Report of a Case in a Seven-Month-Old Child with Impending Suffocation, Operation and Recovery. Nils Lindquist and Helge B. Wulff. J. Thoracic Surg. **16:** 468–476, October 1947.

The authors believe that all mediastinal tumors in children should be removed unless there are specific contraindications. They report the case of a seven-month-old infant with signs of pressure on the trachea, from whom they successfully removed a large enterocystoma located in the right upper posterior mediastinum. This cyst was lined by gastric mucosa as well as some epithelium resembling colon mucosa. A review of the literature leads them to conclude that there are about 80 reported cases of intrathoracic cysts lined with alimentary tract mucosa. Forty of these were mediastinal and lined with gastric, esophageal, or enteric mucosa or a combination of these. The esophageal-lined cysts are smaller and do not appear to endanger life. The clinical course of the others would indicate that mediastinal cysts of foregut origin are rapidly fatal.

The diagnosis depends almost entirely on the roentgen examination. The masses are usually on the right side of the mediastinum, and posterior. Preoperative aspiration of the tumors is advocated by some writers, but is deplored by the authors.

HAROLD O. PETERSON, M.D.

Gastrogenous Mediastinal Cyst. Louis R. Davidson and Lowell Brown. J. Thoracic Surg. **16:** 458–467, October 1947.

The authors present one case of gastrogenous mediastinal cyst because of the rarity of such lesions. This makes 22 such cases now on record. These the authors review.

The lesions are discovered primarily in infants and young children. All but two patients were under five and a half years of age. One patient was fifteen and another twenty-three years old. Fourteen were males, 8 females.

Eighteen of the cysts projected into the right hemithorax and 17 were posterior.

Several cases were asymptomatic.

Aspiration may prove a helpful diagnostic procedure if hydrochloric acid is obtained.

All cases should be operated on to establish the diagnosis and also because the cyst may cause trouble later even though it is asymptomatic when discovered.

In one case the cyst shared a common muscular wall with the esophagus, complicating removal and resulting in an esophagopleural fistula.

HAROLD O. PETERSON, M.D.

Aneurysm of the Pulmonary Artery: Review of the Literature and Report of a Case. Ralph A. Deterling, Jr., and O. Theron Clagett. Am. Heart J. **34:** 471–499, October 1947.

In a collected group of 109,571 postmortem examinations made between 1848 and 1946 in various institutions, there were found only 8 aneurysms of the pulmonary artery, an incidence of 1 in 13,696 necropsies. A collected series of 4,126 reported intrathoracic aneurysms, covering the period 1785 to 1946, showed only 6 involving the pulmonary artery. Observations of individual writers bear out the rarity of the condition.

Accepting as authentic only those cases in which, at necropsy, a permanent, more or less circumscribed dilatation of the pulmonary artery was present with some organic degeneration of its wall, the authors were able to collect from the literature (1860–1934) 35 cases, to which they add a thirty-sixth. They present in tabular form the salient data for these cases and for 23 additional ones diagnosed clinically but not proved postmortem. These examples are in addition to those collected by Boyd and McGavack in 1939 (Am. Heart J. **18:** 562, 1939), numbering 139.

On the basis of their own collected necropsy series, the authors record the following characteristics of aneurysm of the pulmonary artery. It occurs with about equal frequency in the two sexes. The average age for males is 42.8 years, for females 39.3 years. The main pulmonary artery is usually involved (89 per cent). Syphilis played a probable role in 36 per cent. Congenital defects were present in 47 per cent, chiefly patent ductus arteriosus. Mycotic degeneration of the wall of the pulmonary artery was found in 4 cases, and was associated with either an infected patent ductus or subacute bacterial endocarditis with valvular vegetation. Atheroma was mentioned as a significant observation in 11 necropsies. The role of trauma was questionable.

Exertional dyspnea was the most frequent symptom, with cyanosis, edema, cough, hemoptysis, pain, clubbing of fingers and toes, ascites, tachycardia, epistaxis, and underdevelopment occurring with decreasing frequency. A harsh systolic murmur was heard in 19 of the 36 cases (with a separate diastolic murmur in a few); in 8 a distinct thrill was noted.

Enlargement of the heart is believed to depend upon secondary factors. It was mentioned in 31 cases, involving the entire heart in 25 per cent, the right side in 70 per cent, and the left side in 5 per cent.

Roentgenologically the lesion was usually revealed as a discrete rounded shadow at the hilum, which in the oblique view could be outlined beneath the arch and anterior to the aortic outline. The vascular nature of the lesion was confirmed in most instances by fluoroscopy. The peculiar expansile pulsation is transmitted through the lesser radicals of the pulmonary artery to result in what has been described as Pezzi's sign, or the characteristic "hilar dance." Kymography, orthodiagraphy, tomography, and angiocardiography may aid in establishing the diagnosis.

The authors' patient was a 37-year-old white male. The diagnosis was made clinically but a surgical cure was prevented by the extent of the aneurysm. Postmortem, in addition to the aneurysm, there were found atheroma of the right pulmonary artery, bilateral pulmonary arteriosclerosis, a patent ductus arteriosus, and a double subclavian artery.

HENRY K. TAYLOR, M.D.

Interpreting the Electrokymogram of Heart and Great Vessel Motion. B. R. Boone, W. Edward Chamberlain, F. G. Gillick, G. C. Henny, and M. J. Oppenheimer. Am. Heart J. **34:** 560–568, October 1947.

With a special photosensitive pick-up device attached to the patient side of a fluoroscopic screen, a record of

the motion of any portion of the heart and large vessels can be obtained. Points on the cardiovascular silhouette for recording are selected fluoroscopically, and as many cycles of motion as desired are recorded on standard bromide paper with an electrocardiographic recorder.

The electrokymograph complements the work of the roentgenkymograph. It produces records, with adequate detail, of any desired duration and readily lends itself to the simultaneous recording of other cardiodynamic phenomena, as the pulse, electrocardiogram, or stethogram. When such known phenomena are recorded simultaneously with heart motions on the same time axis, significant points on these familiar curves may be projected to the curves depicting the heart motions. The authors have found the carotid pulse tracing most suitable for establishing time relationships.

The electrokymographic record shows expansile or filling phenomena as upward moving limbs, and contractile or emptying phenomena as downward moving limbs. With a standard electrocardiographic recorder the paper speed is 25 mm. per second; the small vertical timing lines are at 0.04 second intervals, and the horizontal lines are 1 mm. apart. Rapid movement is represented by a steep slope, slower movement is represented by a less steep slope, and no movement is represented by a horizontal line. Changes in slope upon a limb represent changes in speed of action. Notches or serrations represent superimposed changes of action due to closure of valves or positional changes.

The recorded movements may be described as consisting of *volumetric* and *positional factors*. For the main part, the movements of the cardiac silhouette reflect volumetric changes. The positional factors have to do with the movements of the heart as a whole during systole and diastole.

A schematic drawing showing the application of the phases of the cardiac cycle to the ventricular kymogram is included. The ventricular curve consists mainly of 2 components, one descending, the other ascending, and each is preceded by a serration. The phases of the ventricular cycle are: isometric contraction; ejection phase; protodiastolic phase; isometric relaxation; rapid diastolic filling, and slowed diastolic filling. The end periods of isometric contraction, of ejection, and of the protodiastolic phase coincide with well defined points on the carotid pulse tracing.

HENRY K. TAYLOR, M.D.

Heart Size in Neurocirculatory Asthenia, Effort Syndrome, or Anxiety Neurosis. Jacques Carlotti, Mandel E. Cohen, and Paul D. White. Am. Heart J. **34:** 552–559, October 1947.

The authors measured from teleroentgenograms the cardiac diameters and areas in 67 patients (mostly soldiers) with neurocirculatory asthenia (50 chronic and 17 acute), and compared them with similar measurements in 50 healthy subjects within the same age group (20 to 30 years) and also with measurements of 22 young men ill for a long time with tuberculosis. The heart diameters in the neurocirculatory group were found to be slightly smaller, but not significantly so, when compared to the group of 50 healthy men. The heart areas were significantly smaller. The patients with neurocirculatory asthenia, however, were smaller in height, weight, and surface area than the men of the healthy control group, and when the heart areas and heart diameters were adjusted for the body surface area of each subject, no significant differences between the two groups were demonstrable. The heart measurements in the tuberculous group were slightly less than those of the neurocirculatory group, but here again correction according to body size reduced the difference. These studies do not reveal valid statistical evidence to support published statements stressing the small size of the heart in neurocirculatory asthenia, if the body size of the individual is taken into consideration.

HENRY K. TAYLOR, M.D.

Reticulum Cell Sarcoma with Cardiac Metastasis: Report of Two Cases with Ante-mortem Diagnosis of One. Irving B. Brick and Maurice Greenfield. Am. Heart J. **34:** 599–611, October 1947.

Two cases of reticulum-cell sarcoma involving the heart and stomach are recorded, with postmortem findings. Surgical exploration in each instance showed the gastric lesion to be inoperable.

In the first case the original diagnosis of reticulum-cell sarcoma was made from an inguinal node biopsy. Subsequently, gastro-intestinal symptoms developed and a large gastric defect was demonstrated roentgenologically. Operation revealed extensive neoplastic involvement of the stomach, and lymph nodes removed from the gastrocolic omentum for examination showed "early transformation into lymphosarcoma, probably reticulum-cell type." Later dyspnea occurred; a chest film showed enlargement of the cardiac silhouette suggesting pericardial effusion and cardiac dilatation; the electrocardiogram indicated a complete A-V heart block. A diagnosis of metastatic involvement of the heart was made and confirmed at autopsy.

The second patient presented clinical evidences of gastric involvement, but there was no roentgen examination of either the chest or alimentary canal. Electrocardiographic examination was also omitted.

The authors quote Yater's suggestion that in every case of heart block, particularly if complete, the possibility of a tumor should be considered. They also strongly support the view of Scott and Garvin that any patient with malignant disease in whom cardiac failure develops should be suspected of having cardiac metastasis.

HENRY K. TAYLOR, M.D.

Prognosis of Patent Ductus Arteriosus. J. Benn. Brit. Heart J. **9:** 283–291, October 1947.

From a study of a group of cases of patent ductus discovered on routine school examination the author concludes that the prognosis is not nearly so gloomy as was previously thought. Since earlier studies were based mostly upon autopsy series or cases seen because of symptoms, this would seem to indicate that many cases exist unrecognized among the general population.

Practically all cases present the characteristic machinery murmur and engorgement of the pulmonary artery and branches. Hilar pulsations are nearly always visible on fluoroscopy; if they are not, it means that the shunt is small. When the shunt is small the heart will not show roentgen evidence of enlargement; with a large shunt it is the left ventricle which enlarges most. The high pulmonary pressure causes some right ventricular hypertrophy. Some cases show retardation of development but many are normal in this respect. Pulse pressure is always high and may be so high as to show a Corrigan type of pulse.

In the author's group of cases found on routine exami-

nation none developed subacute bacterial endocarditis or congestive heart failure during the period of observation, averaging eight years. This is in sharp contrast to Maud Abbott's figures of autopsied cases, with 43 per cent dying of heart failure and 30 per cent of subacute bacterial endocarditis.

Taking into account the efficacy of the penicillin treatment of bacterial endocarditis and the still considerable operative mortality, the author believes that operation should not be undertaken as soon as the diagnosis is made in order to prevent subacute bacterial endocarditis. His indications for surgery are: presence of subacute bacterial endocarditis, recovered bacterial endocarditis, cardiac embarrassment, and poor physique (presumably in children). ZAC F. ENDRESS, M.D.

Cardiac Catheterization in Cases of Inter-auricular Septum, Primary Pulmonary Hypertension, Fallot's Tetralogy, and Pulmonic Stenosis. Sheila Howarth, J. McMichael, and E. P. Sharpey-Schafer. Brit. Heart J. **9:** 292–303, October 1947.

A series of cases of the conditions listed in the title is presented with the data shown by cardiac catheterization and gas analysis, showing the value of this procedure in the demonstration of shunts between the greater and lesser circulations. Nothing new is added but with any new procedure the recording of data by competent observers is always important as a guide for others. Roentgenograms are reproduced in half-page size on each case discussed. ZAC F. ENDRESS, M.D.

Transposition of Aorta and Pulmonary Artery, With Intact Interventricular Septum, Patent Foramen Ovale and Closed Ductus Arteriosus. Béla Halpert and Vernon D. Cushing. Am. J. Dis. Child. **74:** 476–480, October 1947.

A case of complete transposition of the aorta and pulmonary artery with intact interventricular septum, patent foramen ovale, and closed ductus arteriosus, in a 3-month-old boy, is reported. This is believed to be the thirteenth recorded instance of such an anomaly.

Congenital Eventration of the Diaphragm. J. Dewey Bisgard. J. Thoracic Surg. **16:** 484–491, October 1947.

Eventration is defined as an abnormally high or elevated position of one leaf of the intact diaphragm as a result of paralysis, aplasia, or atrophy of varying degree of the muscle fibers. In a broad sense it includes those conditions following surgical interruption of the phrenic nerve or involvement of the nerve by trauma, inflammation, or neoplasm. In a limited sense it includes only cases of congenital or idiopathic origin. A review of the literature in 1935 brought out 183 cases. Probably most cases are congenital. Of the 183 reported in 1935 only 18 were on the right side. During the recent war, at induction centers, 35 cases were discovered during the examination of 412,149 chest roentgenograms of inductees. These cases were entirely or relatively asymptomatic. In infants symptoms are more prominent and consist of respiratory embarrassment, dyspnea, and cyanosis. Symptoms in adults are rare; they include abdominal or chest pain, vomiting, dyspnea, constipation, nausea, belching, loss of appetite, diarrhea, pain on swallowing, cramps, heartburn, dyspnea, cough, wheezing, palpitation, cyanosis, and tachycardia. Physical findings are inconstant except for an increased respiratory excursion of the ribs on the affected side.

Diagnosis is made by roentgenographic examination. There is a conspicuous elevation of the diaphragm in a smooth unbroken curve. The entire diaphragm must be visualized. Barium sulfate in the stomach and colon may be helpful. Motion of the diaphragm may be slight, absent, or paradoxical. Differential diagnosis between eventration and hernia may be difficult, and pneumoperitoneum may be necessary.

Eventration is not often reported in infants. The writer reports a case in a 6-week-old child, on the right side, with dyspnea and cyanosis. At operation the diaphragm was plicated and thus brought down to the 10th rib. Complete relief of the dyspnea and cyanosis followed, and the patient was well twenty-two months later. Four roentgenograms are reproduced including preoperative and postoperative films.

HAROLD O. PETERSON, M.D.

THE DIGESTIVE SYSTEM

The Esophageal Varix. A Report of One Hundred and Fifteen Cases. William H. Higgins, Jr. Am. J. M. Sc. **214:** 436–441, October 1947.

A communication exists between the portal and caval systems by means of the esophageal veins. In portal hypertension there is a tendency to damming back of the blood through the valveless veins to enter the esophageal veins and thence the systemic circulation. The capacity of the esophageal veins, with very little connective-tissue support, is overtaxed, and varices result.

The principle of roentgenographic visualization depends on the displacement of a thin coating of barium by the dilated veins; this is best shown by "spot" radiography. Food particles, cardiospasm, and polyps or other new growths must be excluded.

In a group of 115 cases diagnosed as esophageal varices by roentgenographic, esophagoscopic, postmortem, or clinical examinations, deaths from hemorrhage numbered 51 per cent. Only 18 per cent gave a history of previous episodes of bleeding.

Treatment in the reported cases was only palliative. Portocaval anastomosis is the only physiologically sound procedure. BENJAMIN COPLEMAN, M.D.

Transthoracic Esophogastrectomy, with Reports of Two Cases. Robert I. Hiller. Wisconsin M. J. **46:** 1011–1014, October 1947.

The author states that in point of frequency carcinoma of the esophagus holds fourth place among malignant tumors in men over twenty and that between 30 and 50 per cent of the tumors occur in the lower third. Lesions in the upper third require the Torek operation with permanent gastrostomy. In the lower third or in the cardia of the stomach resection with anastomosis low in the chest is the method of choice.

Early and late symptoms are described and it is stated that the tumors grow rapidly. The history of resection of the esophagus is reviewed.

Two case reports are given in detail, in which immediate surgical results were good. The lesions in these two patients were adenocarcinomas in the lower end of the esophagus and cardia of the stomach.

Early recognition is of the greatest importance and it is pointed out that in both of these cases the lesion was missed in the radiological examination six months before the patients came to surgery.

ALTON S. HANSEN, M.D.

Roentgenological Examinations of Ileus. J. Frimann-Dahl. Acta radiol. **28:** 331–351, Aug. 30, 1947.

This is a detailed discussion of the value of the roentgen examination in ileus. The author's summary in general is as follows: Roentgen studies of an intestinal obstruction give an exact diagnosis in most cases and also show whether the ileus is mechanical or paralytic, or a combination of the two. The site of the stenosis is often seen on the scout films, and in the large bowel the nature of the obstruction is revealed both directly and after a barium enema. An ileus of the small intestine may be diagnosed very early. The roentgen signs are outstanding also in a stage of the obstruction when clinical symptoms are indefinite. In about 5 per cent of cases of ileus of the small bowel, the findings are scanty, but close scrutiny of the films may suggest a strangulating obstruction. An incarcerated loop gives fewer symptoms than a simple obstruction. Repeated examinations are a valuable guide to the surgeon in determining the need for operative interference. The differential diagnosis of ileus and other acute abdominal conditions is also discussed.

The author lists the radiological signs in acute mechanical ileus of the small intestine.

Obstruction and Obturation: Hoop-shaped, gas-filled loops of bowel above the stenosis. Definite fluid levels in motion, especially in subacute conditions. No tumor shadow visible; often fluid-containing loops of small bowel. Little or no gas in the colon; if present, diminishing (increasing gas indicates incomplete stenosis and improvement). Exudate often difficult to see. Free diaphragm. Little deformity of other organs in acute conditions; more in subacute. Patient usually comes relatively late to roentgen investigation, perhaps repeatedly, and ultimately with barium.

True Strangulation: Few small bubbles of gas. Often small fluid levels with little movement (can also be long fluid levels). Tumor-like opacity with multicircular outline. Scanty gas in colon and sometimes in cecum and ascending colon. Abundant fluid, but can be difficult to make out. Diminished movement of the diaphragm. The fluid-filled loops may exert pressure on other organs, *e.g.*, kidneys, ureters, bladder, stomach, and bowel. Patient appears relatively early for investigation because of pain, and barium is seldom used.

Contribution to the Study of Intestinal Invagination. II. Early Diagnosis of Intestinal Invagination by Barium Enema in Infants and Small Children. Ed. Juillard. Schweiz. med. Wchnschr. **77:** 1132–1135, Oct. 25, 1947.

Although operation is the treatment of choice for intussusception in adults and larger children, the author feels that in infants and small children surgery should be reserved for those patients in whom reduction by barium enema fails. He quotes Nordentoft's statistics to the effect that enema reduction was effected in 48.5 per cent of 196 children under fifteen years of age, citing this as evidence in favor of his views. He further illustrates his thesis by reporting 8 cases, of which only 2 were from his own experience, because of the relative rarity of the condition. He notes in this connection that in the year 1941 there was only about 1 case per 200,000 inhabitants in Switzerland; in Denmark the occurrence is eight to ten times as great, with children affected twenty to fifty times as often as adults. The ileocecal type of intussusception is the most common.

LEWIS G. JACOBS, M.D.

A Case of Multiple Hyperplastic Tuberculosis of the Colon. Harald Brodin. Acta radiol. **28:** 227–235, June 30, 1947.

This case report of hyperplastic tuberculosis of the colon is accompanied by a review of some of the literature on the subject. The author points out very well the difficulty in trying to differentiate this lesion from carcinoma. It is concluded that a definite differential diagnosis cannot be made on the basis of the roentgen study.

Hyperplastic tuberculosis of the colon is not a very common lesion and differences in the sundry reports make an estimation of the actual frequency impossible. It is most apt to occur in young adults. The lesions may attain enormous size (as large as a child's head), and a palpable mass is always present. The author feels that it is always a secondary lesion, although the initial infection may be small and hard to find. The clinical history is usually of longer duration than in carcinoma. The lesions may be multiple, as in the author's case, but are not so likely to be multiple as are carcinomatous lesions. There is usually associated irritability of the adjacent bowel, but this is not a constant finding. Pathologically, mesenteric nodes are always involved.

Proof of the lesion is determined by: (*a*) *macroscopic* evidence of solitary or multiple, stenosing, thick-walled, cylindric, hard, often nodose tumors, which may or may not be fixed to adjacent organs; (*b*) *microscopic* demonstration of tubercle formation in the mass with extensive connective-tissue proliferation, principally in the submucosa and subserosa. The regional nodes are almost never free of tuberculosis, and tuberculosis can invariably be detected in the clinical history if careful search is made. JAMES C. KATTERJOHN, M.D.

Foreign Bodies in the Intestinal Tract. Thomas J. Snodgrass. Arch. Surg. **55:** 441–454, October 1947.

This interesting report deals with perforation of the gut by the common toothpick. Twenty cases were found in the literature, and an additional instance is reported. Apparently the wearing of complete dentures, with consequent loss of sensory stimuli in the roof of the mouth and the gums, is a prominent contributing factor to the ingestion of toothpicks. While the x-ray findings are non-contributory, this type of perforation should be kept in mind in the presence of obscure intra-abdominal symptoms. LEWIS G. JACOBS, M.D.

Biliary Fistulae Due to Gallstones, with Report of Two Cases. John R. Cochran and Ralph E. Dolkart. Illinois M. J. **92:** 228–232, October 1947.

The incidence of gallstone ileus, according to available reports, is quite low. Calculi reach the intestine through fistulous tracts at various levels. To cause an obstruction, the stone must usually measure at least 2.5 cm. Its shape also is of importance in this respect, faceted calculi being more prone to cause bowel spasm and obstruction than smoother ones. The most common site of the obstruction is in the duodenum, at the level of the ligament of Treitz, or at the ileocecal valve. Diagnosis is largely dependent upon roentgenography. In patients with intestinal obstruction who present a past history of gallbladder disease, or in patients with an atypical obstruction, a roentgenogram of the abdomen should be taken with particular attention to the right upper quadrant. If gas is seen in the biliary tree,

a presumptive diagnosis of gallstone ileus can be made.

Two cases are recorded. In one, a large calculus was present in the third portion of the duodenum, causing obstructive symptoms. In the other, there was a fistulous tract from the fundus of the gallbladder to the transverse colon, just to the right of the mid-line. Both cases were diagnosed with the aid of the x-ray.

SAVA M. ROBERTS, M.D.

Acute Appendicitis Simulating Gall-Stone Ileus. G. E. Moloney. Brit. J. Surg. **35:** 212–213, October 1947.

This is a case report of a man, aged 50, who gave a history of severe colicky pain in the epigastrium of forty-eight hours duration. About ten hours before admission to the hospital the pain shifted to the hypogastrium, and the symptoms and signs were those of intestinal obstruction. Scout films of the abdomen in sitting and supine positions revealed a definite ileus and also a large laminated opacity in the lower right quadrant. A diagnosis of gallstone ileus was made. At operation a large gangrenous appendix containing a fecalith was found. The appendix lay over the pelvic brim and was adherent to the overlying ileum, thus being responsible for local paralytic ileus. For seven days after operation paralytic ileus continued but was eventually relieved by the Miller-Abbott tube. The fecalith consisted of organic material and calcium phosphate and, on section, had a definite laminated appearance.

MAX CLIMAN, M.D.

Hepatic Calculi. Anthony Bassler and A. Gerard Peters. Am. J. M. Sc. **214:** 422–430, October 1947.

Liver stones have been found in about 6 per cent of cases of cholelithiasis coming to autopsy. The various theories advanced for the genesis of gallstones apply equally to liver stones, which are usually of the bilirubin-calcium type. Since the majority of patients have coexisting stones in the gallbladder and/or bile ducts, it is difficult to describe characteristic symptoms of hepatolithiasis. Fever may be present if the stones are associated with abscesses or cholangitis. The diagnosis is impossible without roentgenography.

Hepatic calculi must be distinguished from hemangiomas, which usually exhibit numerous trabeculations radiating from a common center; amebic abscesses, in which the calcification is dense and irregular; echinococcus cysts, where the calcification in the capsule is in concentric strips alternating with transparent strips; and other lesions, such as tuberculomas.

Four cases are described.

BENJAMIN COPLEMAN, M.D.

THE MUSCULOSKELETAL SYSTEM

On the Problem of Trauma and Aseptic Osteonecrosis. Ivan Hermodsson. Acta radiol. **28:** 257–268, June 30, 1947.

Three cases are reported in an effort to determine whether aseptic osteonecrosis is caused by trauma alone or whether a predisposing factor is necessary. Further, the author attempts to determine whether in aseptic necrosis due to trauma there must be (1) a fracture, or (2) a vascular disturbance of some kind, or finally (3) both a vascular disturbance *and* a fracture.

Case 1 was that of a 13-year-old boy with an injury to the right elbow, causing a vascular disturbance, and a small chip fracture of the proximal ulna on its radial surface. Six to seven months later fragmentation of the humeral capitellum and the head of the radius occurred, with fusion of the fragments after two and a half years. Survey roentgen studies of other bones showed no abnormalities. This case is thought to be one of a vascular disturbance due to trauma with subsequent development of osteonecrosis.

Case 2 was that of a 10-year-old boy who fractured the epiphyseal nucleus of the head of the radius and had an associated fracture of the metaphysis. A septic osteonecrosis did not develop, although a tendency toward its development is indicated by the subsequent occurrence of Schlatter's disease. This case is submitted as evidence against the assumption that a primary fracture as such may cause aseptic osteonecrosis.

The third patient was a 10-year-old boy in whom aseptic osteonecrosis in the fibular malleolus followed primary injury without fracture eighteen months earlier.

The cases presented seem to support the conclusion that aseptic osteonecrosis following trauma can develop without a constitutional tendency toward the disease, and that it is usually due to a vascular disturbance caused by the trauma and not to a primary fracture.

JAMES C. KATTERJOHN, M.D.

Osteoid Osteoma, Review of the Literature and Report of Thirty Cases. Mary S. Sherman. J. Bone & Joint Surg. **29:** 918–930, October 1947.

This article reviews the literature on osteoid osteoma and adds 30 cases to those already reported. The ages of the patients ranged from five to thirty-five years with the greatest incidence between five and fifteen years. Lesions were found in the tibia, femur, astragalus, vertebrae, humerus, toes, fingers, os calcis, ilium, and pubis. Clinically, the patient complains of severe pain, especially at night. The chief clinical findings are tenderness, usually localized, with possibly palpable thickness of the bone. If the lesion is near the joint, motion may be limited or painful.

Radiographically, the lesion is demonstrable as a round or ovoid area of decreased density within which there is often a smaller and denser shadow. There is usually some sclerotic change in the surrounding bone. Sometimes this is so pronounced that the nidus is difficult to demonstrate.

Response to treatment is very satisfactory. Removal of the nidus gives dramatic relief of pain.

The author agrees with Jaffe that osteoid osteoma is a benign bone tumor without any indication of an infectious process.

JOHN B. MCANENY, M.D.

Case of Osseous Changes in a Patient with Hemophilia. Jens Petersen. Acta radiol. **28:** 323–330, Aug. 30, 1947.

Petersen reports a case of hemophilia which showed not only the characteristic roentgen changes in the knee joints but in addition osseous changes recorded in only one previous case (Forfota: Röntgenpraxis **3:** 399, 1931. Abst. in Radiology **17:** 371, 1931). Roentgenograms of the pelvis and hip joints showed in the squama of the left iliac bone a large, cyst-like rarefaction, 9 by 11 cm. in diameter, rather sharply defined medially, where the margin was slightly sclerosed; laterally the demarcation was less sharp and somewhat irregular, and here there was, especially downwards, a distinct expansion of the bone, with irregularly curved contours. In the rarefied portion was seen a faint tra-

becular design. The hip joints showed nothing positively abnormal. In the space between the neck of the femur and the squama of the left iliac bone, extending a little over these, was a faint, irregular opacity, presumably an indication of incipient calcareous deposit. Extending laterally downwards from the left ischial tuberosity toward the lesser trochanter, and branching in the form of a Y around the latter, was a sharply defined calcareous shadow, barely 1 cm. broad. On the interior side of the right hip joint, a similar shadow extended from the upper part of the joint vertically downwards toward the lesser trochanter.

Subsequent examination showed the cyst-like rarefaction to be a little more well defined downwards, and the margin a little more sclerosed. The lateral definition was still somewhat irregular, and one had the impression of increased expansion there. There was now also a rarefied area, about 2 cm. in diameter, immediately below the upper margin of the iliac crest. The calcification between the left femur and the squama of the iliac bone was much more pronounced; the other calcifications were unchanged.

The author believes that the bony changes described are due to subperiosteal or intra-osseous hemorrhages with subsequent cystic development. Roentgenograms are reproduced.

Gaucher's Disease Without Splenomegaly. Margaret E. Morgans. Lancet **2:** 576–578, Oct. 18, 1947.

Splenomegaly is usually considered an invariable and necessary feature of Gaucher's disease. A family with the disease, but in whom none of those so affected showed splenomegaly, is presented. The diagnosis was made by the detection of Gaucher cells in the bone marrow and by the presence of typical radiological lesions in the bones. The family history suggests that in this series the disease was not only congenital but also hereditary. All the patients led active lives, and in one the diagnosis was first made at the age of sixty-seven.

The Sternum of the Child. Actual Frequency of Developmental Disorders Revealed by Radiographic Examination. Herdner. J. de radiol. et d'électrol. **28:** 387–393, 1947.

During a period of several years, the sternums of several hundred children were examined by means of tomography. The author states that no other bone shows more clearly the state of ossification than the sternum. The centers of ossification are juxtaposed in a single plane contiguous to the mid-line and the centers on the right parallel those on the left, thus permitting comparative examination of the development of both sides.

Throughout the early years of the study, examination of weak, undernourished children, for the most part between the ages of four and twelve, revealed only abnormalities of development of the body of the sternum. These fell into two groups, which were often combined: (1) retardation of transverse union of the centers of ossification, and (2) irregularity of development of these centers.

Normally, the manubrium develops from one center of ossification. In 1946, there suddenly appeared, in a series of children under ten years, multinucleation of the manubrium, varying from simple binucleation to four or five points of ossification. The author is aware of the frequent anomalies of development of the sternum in normal individuals but feels that because of the frequency of a condition not seen before 1946, these findings indicate grave deficiencies of growth the result of food rationing during the war and enemy occupation. Of children under ten years, referred in general for pulmonary examination, two-fifths showed retardation as manifested by the manubrium.

RODERICK L. TONDREAU, M.D.

Spontaneous Fracture of the First Rib Due to Muscle Pull. A Case Report. A. Waxman and H. Geshelin. California Med. **67:** 243–244, October 1947.

Spontaneous fractures of the first rib due to muscle pull are rare, only 7 cases having been reported to date. The fractures are attributed to contracture of the scalenus anticus muscle during physical stress. Pain may be minimal or absent. There are no complications and healing takes place by callus or pseudarthrosis. The author reports a case. MAURICE D. SACHS, M.D.

Backward Displacement of Fifth Lumbar Vertebra in Degenerative Disc Disease. The Significance of the Difference in Anteroposterior Diameters of the Fifth Lumbar and First Sacral Vertebrae. Gilbert H. Fletcher. J. Bone & Joint Surg. **29:** 1019–1026, October 1947.

The author's object is to demonstrate that posterior displacement of the fifth lumbar vertebra on the first sacral segment is a definite pathological process. It is not a separate entity, but a mechanical consequence of degenerative disk disease. This study is based upon 600 roentgenograms of the lumbosacral spine from cases in which backache was the chief complaint. In 39 of the patients, advanced degenerative disk disease was found, this diagnosis being based on the presence of a narrowed disk associated with sclerosis, hypertrophic change, umbilication on the lower surface of the fifth lumbar body, and subdislocation of the facets. In some of these cases the lower surface of the fifth lumbar body actually rested upon the posterior edge of the first sacral segment.

It is believed that the backward displacement is due to the narrowing of the disk and that slipping of the facets does not occur without backward and downward displacement carrying the fifth body backward in its relationship with the first sacral segment. The amount of displacement is considered to depend somewhat upon the obliquity of the facets.

Patients with backward displacement of the fifth lumbar vertebra with the herniated disk syndrome received little benefit from the ordinary procedures used in treating herniated intervertebral disks. It is the author's feeling that a fusion of the lumbosacral joint will relieve the pain in these patients.

When malalignment of the fifth lumbar and the first sacral segment appears to be present, the lower surface of the former and the upper surface of the latter segment should be measured. If the malalignment exceeds the difference in diameters, there is actual backward displacement. JOHN B. MCANENY, M.D.

Postspinal Headache. Etiology and Prophylaxis. Aidan A. Raney and Rupert B. Raney. West. J. Surg. **55:** 550–554, October 1947.

Headache has been reported as a sequel of spinal puncture in 5 to 25 per cent of patients. This has usually been attributed to leakage of spinal fluid, but

the authors do not believe that to be the responsible factor. They believe that in most cases a cervical disk lesion is the basis of the trouble and that the placement of the patient in marked flexion with resultant strain on the neck is the precipitating factor. A careful history with reference to disk symptoms should be taken preceding spinal puncture and when these are found undue flexion and manipulation should be avoided.

Far too often in the investigation of so-called post-spinal headache, films of the cervical spine are not taken, with the unfortunate result that a psychogenic label is attached to the patient's complaints.

MAURICE D. SACHS, M.D.

Two Cases of Vertebral Osteochondritis: Infantile and Adolescent (Radio-Clinical Study). Pierre Ingelrans and A. Vendeuvre. J. de radiol. et d'électrol. **28:** 398–401, 1947.

The authors report two cases of vertebral osteochondritis, one in a boy of 13 years with involvement of the tenth thoracic vertebra, the other involving the twelfth thoracic vertebra in a child of 3 years. A review of the literature by Péchoux in 1936 revealed 19 such cases reported between 1925 and 1936. The authors list the characteristics of this disease as described by Calvé in his original article in 1924 (see Abst. in Radiology **6:** 446, 1926). RODERICK L. TONDREAU, M.D.

On Tibia Recurvata. H. B. Goettsch and M. de Grood. Acta radiol. **28:** 254–256, June 30, 1947.

The authors have observed 3 cases of painless, symptomless *tibia recurvata* in the short period of four years. This report follows a previous report of idiopathic symptomless *tibia recurvata* by Karen Lübschitz (Acta radiol. **27:** 81, 1946. Abst. in Radiology **48:** 102, 1947). In all of these patients there is a zone of increased density at the most distal end of the *apophysis tibiae*, the site of a definite epiphysis in normal growing persons. It is suggested that too early ossification at this point causes the lesion. Surgical correction is possible. JAMES C. KATTERJOHN, M.D.

Marfan's Syndrome in the Adult. Dissecting Aneurysm of the Aorta Associated with Arachnodactyly. John R. Tobin, Jr., Emmet B. Bay, and Eleanor M. Humphreys. Arch. Int. Med. **80:** 475–490, October 1947.

The clinical characteristics of arachnodactyly (Marfan's syndrome) are discussed, particularly as manifested in adults. The significant lesions in the only 12 autopsied cases of arachnodactyly recorded in the literature (from over 200) are tabulated; 7 of these autopsies were performed on adolescents or adults. Cardiovascular lesions are common and especially important. They include aortic medial necrosis and endocardial lesions which simulate those of rheumatic fever. Clinical data and necropsy findings are presented for 2 additional adults with arachnodactyly, both of whom died as the result of dissecting aneurysm of the aorta.

GYNECOLOGY AND OBSTETRICS

X-ray in Rupture of the Uterus. G. W. Mylks, Jr., A. B. Brown, and W. A. Jones. Canad. M. A. J. **57:** 337–340, October 1947.

Although the authors could find no mention in the literature of the roentgen diagnosis of ruptured uterus, they believe that a soft-tissue film of the abdomen may be of value in cases in which the diagnosis is not clear-cut. The significant finding is the presence of fetal parts lying outside a round soft-tissue mass, which is the contracted uterus. A case is reported in which such a picture was obtained, confirming the clinical impression of a ruptured uterus. Obviously the rupture must be complete, with the fetus either wholly or partly outside of the uterus.

[Hysterosalpingography as a diagnostic aid in certain cases of ruptured uteri has been reported by Sheffery (Am. J. Obst. & Gynec. **49:** 423, 1945. Abst. in Radiology **46:** 100, 1946.)—ED.]

MORRIS IVKER, M. D.

Visualization of the Maternal Circulation at the Site of the Placenta (Placentagrams). Preliminary Report. Leo J. Hartnett. J. Missouri State M. A. **44:** 754–756, October 1947.

Aortograms for the visualization of the aorta and its branches during pregnancy are usually completed before much of the solution has reached the vessels at the placental site. The author reports briefly a series of 11 cases in which the time of exposure was delayed and an outline of the maternal vessels at the placental site was obtained. He does not mention the time factors. A study of the maternal and fetal effects of the procedure is in progress. Roentgenograms are reproduced but can hardly be considered adequate technically.

ERNEST S. KEREKES, M.D.

Causes and Treatment of Tubal Occlusion. Linton Snaith. J. Obst. & Gynaec. Brit. Emp. **54:** 607–618, October 1947.

In a series of 800 cases of infertility, tubal occlusion was known to have been present in 130 patients and was suspected in many others. In 60 cases the occlusion was complete. Pregnancy subsequently occurred in 30 patients who had shown evidence of significant tubal occlusion, complete or partial; hormones played an important part in the treatment of 11 of these, and 3 were subjected to major surgery. Twenty women became pregnant after insufflation or lipiodol, combined with hormone therapy in some cases. Of all cases of sterility, 28 per cent of the successful cures followed insufflation or lipiodol, though it is not certain that this procedure was responsible for success in all cases.

THE GENITO-URINARY SYSTEM

Papillomatous Disease of the Renal Pelvis. Jas. B. Macalpine. Brit. J. Surg. **35:** 113–132, October 1947.

This paper reviews 19 cases of papillomatous disease of the renal pelvis collected over a period of twenty-nine years and includes 17 case reports with excellent reproductions of pyelograms and color photographs of surgical specimens. Two cases occurring in workers in an aniline dye factory are dealt with in a special article in the same issue of the journal (pp. 132–134). Hematuria was the outstanding symptom in all cases. Pyelograms were diagnostic with 2 exceptions. Six cases were first seen by the author after nephrectomy, with secondary growths in the ureter, and in 4 of these there were also vesical implants. Five cases proved to be malignant, with 3 fatalities.

Papillomatous tumors differ from the solid tumors of the upper urinary tract by their mode of spread to the

ureter and bladder. The pathologist's report is not always final as to malignancy as it is impossible to be sure that every portion of a large growth has been examined and that no carcinomatous area has been missed. A growth may be benign in its early stages but become malignant later. This occurred in 2 of the reported cases, in which there were nine- and twelve-year histories of hematuria, respectively. Whenever papillomatous material is implanted in a wound, whether the growth in its original location be benign or malignant, the implant will behave as a malignant one.

Hematuria dominates the clinical picture. Pain is little in evidence in these pelvic tumors. An enlarged kidney was found in 6 of the author's cases and in 3 was due to tumor. In 2 cases tumor and hydronephrosis together were responsible for the renal enlargement, and in only 1 case was the swelling solely hydronephrotic. In this connection it is mentioned, as a diagnostic point, that a hypernephroma rarely if ever causes hydronephrosis. Demonstration of a hydronephrosis in a suspected case of tumor is evidence of pelvic origin.

Cystoscopic examination proved to be of great value in diagnosis both for detecting hemorrhage and ureteral implants at the vesical orifice. The indigo-carmine test was extremely valuable; the dye was absent in 5 cases and its return was delayed in 5, from one minute to twelve minutes.

Pyelography was not diagnostic when the growth was very small. Varying degrees of obstruction arise sooner or later, the onset varying with position of the tumor. Complete obstruction not only to the passage of the catheter up the ureter but also to the introduction of the opaque medium is very suggestive. The most valuable of all pyelographic signs is a filling defect isolated from the external calycine boundary of the pelvis, which differentiates it from the defect produced by a parenchymal tumor. When the pelvis is completely filled with tumor it will admit of neither ascending or decending pyelography. Ureterography has not been of value in diagnosis of secondary ureteric involvement.

Nephro-ureterectomy, either in one or two stages, is the treatment of choice. If the kidney is grossly enlarged the author prefers to let the ureteric precede the renal operation. The importance of avoiding contamination of the wound by particles of tumor is emphasized. The terminal ureter is usually more heavily involved than any other part and must be incised flush with the bladder and means must be employed to ensure the destruction of seedlings within the intramural ureter.

Of the author's 10 patients with "benign" papillomata, 8 are alive and well. The other 2 died after ten and eleven and a half years, respectively, with local recurrences attributed to operative implantations. Only 1 of the 7 patients with lesions recognized as malignant is alive, after a period of six years. The 2 aniline dye tumors are not included in these results.

MAX CLIMAN, M.D.

Studies on Translumbar Aortography. A Simple Apparatus for Aorteriography. A. E. Vitt and W. F. Melick. J. Missouri State M. A. **44:** 749–754, October 1947.

The authors review the literature on translumbar aortography and describe the apparatus and technic. The only medium that has given satisfactory results is 80 per cent sodium iodide, though there would appear to be some danger associated with its use and the pain incident to its injection requires an anesthetic. An x-ray machine capable of a 0.2 second exposure is necessary, and a high-speed Bucky is essential. For the actual injection the authors use a special device made primarily for the injection of sodium pentothal—a 50 c.c. syringe with Luer lock, high-pressure tubing fitted with Luer lock connections, and a 15 cm., 18 gauge steel needle.

Aside from the danger of acute iodism, which is lessened by the intravenous administration of saline following the procedure, the two real dangers seem to be the injury to the aorta and to contiguous structures while trying to locate the aorta. Arteriosclerosis with atheromatous plaques and hypertension seem to enhance the incidence of hemorrhage or hematoma.

There are three types of cases in which one is justified in using aortography at present: (1) those in which one cannot decide the status of a kidney by excretory pyelograms, because of poor function, and a ureteral catheter cannot be passed, due to obstruction; (2) tumors of the kidney producing some clinical manifestation, such as bleeding, but not large enough to produce pyelographic deformity; (3) suspected renal ischemia causing hypertension. The aortogram and the renogram give a clear cut picture of the size of each renal artery as well as the over-all size of the kidney.

Much remains to be done as far as the interpretation of the aortogram is concerned. There are, however, certain findings which are said to be typical and diagnostic. Renal cortical carcinomas commonly show a pooling of the medium in the vascular sinuses found in these tumors. Retroperitoneal tumors show normal renal vascular beds which may be displaced. As has been previously pointed out, aortography may lead to better conservative handling of hydronephrosis for, if the arterial supply of a kidney is adequate, an attempt to save it is worth while.

The article contains a reproduction of an aortogram and an illustration of the apparatus used.

ERNEST S. KEREKES, M.D.

GENERAL CONSIDERATIONS; TECHNIC

American Radiology. Its Contribution to the Diagnosis and Treatment of Disease. George W. Holmes. J. A. M. A. **135:** 327–330, Oct. 11, 1947.

This paper presented as the Centennial Address before the Section on Radiology of the American Medical Association is a summing up of the achievements of American radiology by one who has played a major part in the development of the specialty.

Recent Advances in Radiology. Bertram V. A. Low-Beer. West. J. Surg. **55:** 562–569, October 1947.

As the title indicates, this is a review of recent progress in radiology. Much of the work cited has appeared in RADIOLOGY in the form of original papers or abstracts.

Value of X-rays in the Study of Postoperative Emergencies and Complications. James T. Case. Am. J. Surg. **74:** 414–427, October 1947.

Twenty-one cases are presented illustrating certain abdominal conditions in which diagnosis can be made or assisted by the application of roentgen study. The author points out many useful criteria for diagnosis in his analysis of the various cases.

Localization of intra-abdominal abscesses can frequently be accomplished by study of plain roentgenograms of the abdomen. In doubtful or borderline cases the localization can be further aided by the administration of umbrathor as an opaque medium. This material, which is an aqueous solution of thorium dioxide, is given orally and has practically as good opacifying qualities as barium and the further advantage that it remains in a liquid state at all times.

The recognition of air under the diaphragm may be utilized in appropriate cases as a cardinal sign of rupture of a hollow viscus such as a duodenal or gastric ulcer, an ulcer of the colon, etc. This sign should be interpreted with reserve for there are other conditions under which it may be encountered, such as following operations and after insufflation of air into the peritoneal cavity through the uterine canal as a test of tubal patency.

Criteria for a diagnosis of subphrenic abscess include elevation and fixation of the diaphragm on the affected side, basal pleurisy, and the presence of gas supernatant above fluid in the abscess. The latter sign may not be present but if found is a valuable indication. Various positions of the patient with relation to film and tube should be used to elicit the sign.

Cholecystography and cholangiography are of much help in surgery of the biliary tract. The latter procedure may be done during operation or postoperatively.

Diagnosis of liver abscess sometimes can be made in no other way than the use of thorotrast intravenously. Objection to this medication has been raised due to the fact that it is taken up by the reticulo-endothelial cells of the liver and spleen and retained there for the life of the patient. However, Yater has demonstrated that a single injection of 25 c.c. of a 25 per cent colloidal preparation of thorium dioxide (thorotrast) is well within safe limits.

Following operations upon the stomach, many surgeons find roentgen studies useful to demonstrate the modified form of the stomach, the position of the anastomosis in relation to the stump of the stomach, and the time required for gastric clearance.

X-ray examination is also of value in helping to diagnose intestinal obstruction. This can be done by determining the amount and distribution of gas in the plain films of the abdomen made with the patient in several positions. In some cases the findings may be inconclusive and it has been the author's practice to employ umbrathor orally in such cases.

As regards small intestinal intubation, the author cautions that the history, physical findings, and x-ray studies be carefully correlated and evaluated so that the possibility of gangrene accompanying mechanical obstruction is not overlooked and a fatal delay in operation allowed.

This article should be of particular interest as representing the opinions of the radiology department of Northwestern University Medical School on the use of materials such as thorotrast and umbrathor and as presenting many useful procedures in the application of diagnostic roentgenology to surgery.

MARLYN W. MILLER, M.D.

Statistical Problems in Assessing Methods of Medical Diagnosis, with Special Reference to X-Ray Techniques. Jacob Yerushalmy. Pub. Health Rep. **62:** 1432–1449, Oct. 3, 1947.

The effectiveness for tuberculosis case finding of 35-mm. fluorograms, 4 × 10-inch stereoscopic fluorograms, 14 × 17-inch paper roentgenograms, and 14 × 17-inch celluloid roentgenograms is compared in a study on 1,200 persons, each of whom was examined by all four methods. Independent interpretation was made by five expert radiologists and chest specialists, with a second independent reading of the 14 × 17-inch celluloid films by each. A statistical method was devised to compare results without designating any one technic as the standard, using the evidence yielded by all five readers. (The designation of any method as a standard is objectionable since all errors made are attributed to the "compared" data, even though the error is in fact in the standard data.) The result of this study is to show that, strictly on the basis of the ability to find cases of tuberculosis in mass survey work, none of these technics, not even the 14 × 17-inch celluloid films, is superior to any of the others.

[*Note:* While the author's mathematical methods do not lend themselves to abstracting, the work presented is very careful, and the conclusions presented seem proved beyond a doubt. This work might well serve as a model of "good" medical statistics.—L. G. J.]

LEWIS G. JACOBS, M.D.

Simultaneous Use of the Mobile Anti-Diffusion Grid in Roentgenography of Certain Areas. R. Hickel. J. de radiol. et d'électrol. **28:** 409–410, 1947.

The author attempted to improve contrast of radiographic images by utilizing the following procedure: A metallic 30 + 40 Lysholm grid is placed on a film cassette (or inside the cassette) which, in turn, is placed in the drawer of an ordinary Potter-Bucky diaphragm. The stationary grid is placed so that the opaque strips are perpendicular to the lead sheets of the mobile grid.

Radiographs of bone and viscera were obtained. The combined usage of the two grids did not seem to be of value in the examination of the shoulders, knees, spine, cranium, urinary, or digestive tracts. As far as the cranium is concerned, the exaggeration of contrast produced loss of detail. On the other hand, the use of the two grids simultaneously appeared to be of definite advantage in radiography of the pelvis, where the images were clearly better than when the mobile grid was employed alone. RODERICK L. TONDREAU, M.D.

Micro-Arteriography. A. E. Barclay. Brit. J. Radiol. **20:** 394–404, October 1947.

In the course of studies of the intrarenal vascular system in experimental animals, the ordinary radiographic technics were found to be inadequate for the demonstration of the more minute vessels. Accordingly, a technic was developed whereby micro-arteriograms are obtained which are capable of enlargement without loss of detail up to 250 diameters. The two essentials are a very fine grain film and soft radiation. The film used is capable of resolution up to 1,000 lines. Since the ordinary x-ray tube will not produce soft enough radiation, a diffraction tube with a molybdenum target and beryllium window was used. The most satisfactory media for injection were found to be thorotrast and colloidal gold or silver. The specimen requires special mounting directly on the film. The radiographs obtained are highly selective, showing virtually nothing except the radiopaque material in the vessels. Several excellent illustrations are presented. SYDNEY J. HAWLEY, M.D.

RADIOTHERAPY

Carcinoma of the Thyroid. J. M. Graham and R. McWhirter. Proc. Roy. Soc. Med. **40:** 669–680, September 1947.

Observations for this report were based on a series of 144 unselected cases of thyroid carcinoma from the files of the Royal Infirmary, Edinburgh. They showed a ratio of 1 male to 3.6 females and an average age of 59.75 years. The youngest patient was eighteen and the oldest was ninety-three. In 97 cases the diagnosis of malignant disease was confirmed by histologic examination; in the remaining 47 cases it was made on clinical grounds. In 23 per cent of the series there was a history of previous goiter. The cases were subdivided into three histologic groups: adenocarcinoma 23 per cent; papillary adenocarcinoma 16 per cent; and undifferentiated carcinoma 61 per cent.

This survey was not limited to early operable cases but included all cases referred to a large general hospital. In 53 per cent only palliative treatment or no treatment at all was given. The series, as noted above, contained a high proportion of undifferentiated carcinoma. Of this latter group of patients, 25 per cent died within one month and 50 per cent within four months after they were first seen in the hospital.

The survival rate was not higher in those cases in which the diagnosis was established on clinical grounds alone than where the diagnosis was confirmed histologically.

Operable cases numbered 29, of which 7 were treated by complete thyroidectomy and the remainder by subtotal thyroidectomy. Eighteen of the operable group received postoperative x-ray therapy. Eleven of the 29 patients were alive at the end of five years. Of these, 4 had received immediate postoperative irradiation and 6 were subsequently treated by x-rays for recurrences after treatment by surgery alone. Of 84 *inoperable cases without evidence of distant metastases,* only 39 could be said to have received adequate x-ray therapy. Of this more limited group, 29 per cent were alive after five years. Patients first seen with distant metastases and recurrences were all dead.

Results according to the histologic type of tumor were as follows: Of the adenocarcinoma group, 46 per cent were alive at the end of five years; of those with papillary adenocarcinoma 40 per cent were alive at the end of five years. These numbers are small, however, and the authors caution that they should be accepted with reserve until larger numbers have been treated. For undifferentiated carcinoma the five-year survival rate was 14 per cent, and as no patient treated by surgery alone survived, the favorable results must be attributed to x-ray treatment.

X-ray treatment until recently was given to the thyroid through two opposed lateral fields, with 3,500 r delivered to the tumor in three weeks or less. A single anterior field was used to treat retrosternal carcinomata and retrosternal extensions of a carcinoma in the neck. It was noted that when local response to x-ray treatment was good, local recurrences did not take place but the results were poor because of the high tendency of these tumors to metastasize to the lungs. It was decided, therefore, to treat all undifferentiated carcinomas, as they were found to be highly radiosensitive, by wide-field x-ray therapy in an effort to raise the five-year survival rate, and the immediate responses to this type of treatment are regarded as promising.

The authors conclude that x-ray therapy is not too successful with adenocarcinoma or papillary adenocarcinoma and that surgery gives better results, but deem it wise to continue its use postoperatively, as their observations were made on a limited number of cases.

GLENN F. MILLER, M.D.

Treatment of Lymph Node Metastases from Intra Oral Carcinomas with Special Regard to the Indications for Total Neck Dissection. Rolf Weyde. Acta radiol. **28:** 367–385, Aug. 30, 1947.

The indications for neck dissection in intra-oral carcinoma are discussed on the basis of the re-examination of the Norwegian Radium Hospital's material from 1932 to 1941, comprising 386 histologically verified cases. Three- and five-year results, the causes of death, the development of lymph node metastases, and the results of neck dissection were studied. The total material is divided into the usual three stages according to the presence and extent of lymph node metastases, regardless of the size of the primary tumor: Stage 1, no clinical symptoms of lymph node metastases; Stage 2, clinical metastases, limited and operable; Stage 3, lymph node metastases (*a*) with beginning fixation, (*b*) with infiltration into the surrounding structures, (*c*) bilateral, operable or inoperable. In the series, 224 tumors were Stage 1, 78 Stage 2, and 84 Stage 3.

Treatment of carcinomas of the oral cavity is started by irradiating the primary tumor with teleradium from 1 or 2 or more fields according to the size of the lesion and its situation. The teleradium apparatus is the latest model Sieverts, containing 3.0 gm. of radium and giving a skin dose of 225 to 460 r per hour depending on the size of the area treated and focus distance. The usual daily dose measured on the skin is 530 r, which may be obtained by irradiation for one and a half hours. An attempt is made to get a uniform irradiation of the tumor and the surrounding tissue up to a tumor dose of 4,500–5,000 r, attaining a favorable reaction on the mucous membrane. The primary lesion is re-examined after a period of six to eight weeks. If any part of the tumor remains, it is coagulated or implanted with radium needles or both. The radium needles used contain 10 mg. of radium, with 1 mm. platinum filtration. These are placed 0.75 to 1.0 cm. apart and left for twenty-four hours. In certain types of tumors other surgical treatment may be employed after the lesion of the mucous membrane has been treated radiologically.

Treatment of the regional lymph node areas is begun at the same time as the treatment of the primary tumor by including the adjacent lymph channels in the area of irradiation, thus giving the full tumor dose. Otherwise no prophylactic irradiation is given in Stage 1 and no prophylactic neck dissection is performed. Neither is neck dissection performed immediately in Stage 2 cases. Suspected nodes are included in the irradiation of the primary tumor or are irradiated separately. If the lymph node tumor has entirely disappeared after eight weeks, the patient is kept under observation. If, on the other hand, a remnant of the tumor is still present, total neck dissection is performed unless there are contraindications to surgery and if the primary tumor is free of symptoms or is considered curable by further treatment.

In Stage 3 cases greater individualization in treatment is necessary. In these cases also, treatment is started

with irradiation. Teleradium is used if the tumor is limited and roentgen irradiation of cervical areas if metastases are extensive. Whether neck dissection is to be carried out is decided at the end of eight weeks.

Of the series of cases reported here, 298 were observed for five years or longer, and of these, 23.4 per cent were free of evidence of disease after that period. The three-year figure, based on the total number of patients, is 25.8 per cent (Stage 1, 43.2 per cent; Stage 2, 5.4 per cent; Stage 3, 1.2 per cent).

Papillary Cystadenolymphoma. Karl-Gunnar Tillinger. Acta radiol. **28:** 241–253, June 30, 1947.

The literature is partially reviewed, and 9 cases of papillary cystadenolymphoma, a relatively rare salivary gland tumor, are reported. This tumor appears in men six times as frequently as in women and is found chiefly in the older age groups, though one example has been recorded in a child of seven. The parotid gland is usually involved; less frequently the submandibular gland. The microscopic appearance is characteristic, and upon it the diagnosis depends. The lesion is an epithelial one with areas of lymphatic cells.

The tumor grows slowly and usually forms a distinct capsule. It is easily excised surgically, and only two instances of postoperative recurrence have been reported. Malignant change has been said to occur, but no proved examples have been published. In the series reported here, from the Radiumhemmet, various combinations of surgery and irradiation, preoperative and postoperative, were tried. No recurrences had been observed in periods ranging from less than a year to ten years after treatment. From these results, one might conclude that surgical excision with roentgen or radium therapy is the treatment of choice for this unusual tumor.

JAMES C. KATTERJOHN, M.D.

Radiotherapy for Gynecologic Cancer. Manuel Garcia and Joseph V. Schlosser. New Orleans M. & S. J. **100:** 141–148, October 1947.

Of 17,635 admissions for cancer at the Charity Hospital of Louisiana (New Orleans) between 1928 and 1937, 27 per cent represented neoplasms of the female pelvic organs. Furthermore, a study of the 7,630 admissions for cancer of the cervix in the period 1904 to 1944 demonstrated a steady upward trend in the absolute number of women coming for treatment. The authors believe that alertness in diagnosis, followed promptly by correct treatment, offers a very hopeful outlook for these patients. Various method of treatment are discussed, and their advantages set forth.

For *cancer of the cervix*, radiation therapy is the method of choice, presupposing complete diagnosis and thorough irradiation, including radium application with a field intensity of gamma radiation encompassing the whole primary tumor and its immediate neighborhood and external roentgen therapy administered with the intent of irradiating adequately all potential tumor sites in the lateral half of the parametria and the nodes along the pelvic wall. Since the sole object of the external irradiation is to supplement the dosage along the lateral half of the parametria and in the region of the pelvic walls, it may be given with small fields anteriorly and posteriorly so directed that the cervix itself, the rectum and bladder, and the femoral neck do not lie in the path of the x-ray beam. In this manner the incidence of primary irritative reactions in the intestine and urinary tract and late sequels can be kept at a minimum. This technic is feasible with 200-kv. equipment provided long distances and adequate filtration are employed. The required dosage need not exceed 3,000 r at the tumor region with the treatment delivered over a course of twenty-four to thirty days. In a series of 126 colored women with cancer of the cervix an absolute five-year survival rate of 40 per cent was obtained.

In relatively limited *carcinomas of the urethra and vagina*, control of the disease can be obtained by the use of an interstitial radium implant by the method of Paterson and Parker, administering approximately 6,000 r (gamma) in seven days. This should be supplemented by external x-ray therapy as in carcinoma of the cervix. Of the authors' series of 33 carcinomas of the vagina, half were treated more than three years ago and in 7 of these a three-year arrest of the disease was obtained.

In *endometrial carcinoma*, the authors place the five-year salvage in operable cases treated by radical surgery at between 50 and 60 per cent. These results they believe can be improved by 10 to 15 per cent by combining radium therapy with surgery. The most advantageous time for the introduction of radium into the uterine cavity is at the time of the diagnostic curettage, for an exposure of 3,600 to 4,000 mg. hr. The surgical procedure should then be performed six weeks later, and after convalescence external x-ray therapy should be instituted. In inoperable cases of fundal carcinoma, reliance must be placed entirely on adequate radiotherapy, mostly for palliative purposes. This includes radium application, followed in a month by external x-ray therapy. The results under these circumstances are equally as good as those of surgery alone.

Ovarian tumors are primarily a surgical problem. *Carcinoma of the vulva*, also, is usually treated surgically, though in well circumscribed and superficial lesions and those in which operation is inadvisable radium therapy may be undertaken with good prospects for success. Doses must be moderate. Cases of vulvar carcinoma unsuitable for surgery or irradiation can be benefited by moderate amounts of external x-ray therapy.

A number of illustrative cases are presented with details of treatment and management. A bibliography is appended.

SAVA M. ROBERTS, M.D.

Carcinoma of the Cervix. J. Elliott Scarborough and Robert L. Brown. J. M. A. Georgia **36:** 385–392, October 1947.

This paper is based upon 196 cases of carcinoma of the cervix treated between the years 1937 and 1946.

Abnormal vaginal bleeding is pointed out as the most important early symptom of cervical carcinoma. In only 13 patients did it fail to occur, and in 11 of these a vaginal discharge was present. In 99.5 per cent of all cases definite symptoms pointing to pathologic changes in the pelvis were present. The importance of the history, a careful physical examination, and biopsy is emphasized.

The plan of treatment most frequently employed consisted of external irradiation through two anterior and two posterior pelvic ports, with 200 kv., 0.5 mm. Cu + 1.0 mm. Al filter, 70 cm. target-skin distance. A total dose of 1,500 r is delivered to each of the four pelvic ports and an intravaginal portal, directed to the cervix, is given up to 1,600 r. Two weeks following completion of external irradiation, radium capsules in tandem are

applied in the cervical canal and uterine cavity for a dose of 3,000 mg. hr.

It is felt that surgical treatment should be carried out only in very early cases that are excellent surgical risks. Only one case in this series was so treated.

Complications due to radiation therapy in carcinoma of the cervix are briefly discussed.

Seventy-seven of the cases in the authors' series were treated more than five years ago, and all of these have been traced. In 11 cases in which half or less of the cervix was involved, the five-year-survival rate, with absence of disease, is 100 per cent. Of 12 patients with more than one-half of the cervix involved but without extension beyond the cervix, 75 per cent are free of disease after five years. For those cases with clinical parametrial extension but without complete fixation, the five-year survival is 53.3 per cent. For cases with vaginal extension without parametrial involvement, the figure is 28.6 per cent, and for those with vaginal and parametrial involvement without complete fixation or distant metastases, 22.2 per cent. No patient with far-advanced disease survived five years.

The relationship of symptoms, grade of the lesion, and clinical extent of the disease to the end results is summarized.

ALTON S. HANSEN, M.D.

Carcinoma of the Cervix in the Young Age Group. J. H. Holzaepfel and P. J. Reel. Ohio State M. J. **43:** 1047–1049, October 1947.

This paper is based upon a study of 22 patients under thirty years of age with carcinoma of the cervix seen between 1936 and 1946. Abnormal bleeding, usually painless, and leukorrhea are the most frequent presenting symptoms, and these should be recognized as of significance in younger women as well as in the postmenopausal period.

Microscopic studies were made in each of the cases of this series. Twenty showed squamous-cell carcinoma and the remaining 2 adenocarcinoma arising from the glandular mucous membrane of the cervical canal. The clinical classification was as follows: (*a*) limited to the cervix; (*b*) parametrial involvement with mobile uterus; (*c*) parametrial involvement with fixed uterus; (*d*) extension to vaginal vault; (*e*) massive pelvic involvement; (*f*) metastases, remote. In addition, Broders' index of malignancy—Grades I to IV—was used.

Ten patients were classified clinically in the group with disease limited to the cervix (*a*). In 7 of these the growth was of Grade III malignancy, while the others were listed as Grade II, Grade IV, and carcinoma *in situ*. Eight of this group are living and well and 2 have died of carcinoma. The longest survival at the time of the report was six years. This patient was treated by destructive cauterization of the cervix followed immediately by radical hysterectomy. Five others were treated by a combination of radical surgery and irradiation—preoperative or postoperative radium and deep x-ray therapy. The two patients who died were not considered suitable for surgery.

Of the 3 patients with parametrial involvement not of sufficient degree to immobilize the uterus (*b*) one was alive without evidence of disease six years following radical surgery and postoperative radium (2,400 mg. hr.) and roentgen therapy (2,700 r). Of the 4 patients with immobilization of the uterus (*c*), 2 had died, one refused treatment, and one was alive after fifteen months without gross evidence of disease. Results in the remaining cases are not significant.

The plan of treatment in the Class *a* cases has been to administer 4,000 to 6,000 mg. hr. of radium to the cervix, with radical hysterectomy in suitable cases after six to eight weeks and roentgen irradiation, up to 8,000 r via multiple ports beginning two weeks postoperatively.

Vaginal smears have been found useful for the demonstration of early recurrences.

ALTON S. HANSEN, M.D.

Improvement of Results in the Treatment of Uterine Cancer. J. Heyman. J. A. M. A. **135:** 412–416, Oct. 18, 1947.

The author presents the results of treatment of 842 patients with cancer of the uterine corpus and 4,611 patients with cancer of the uterine cervix observed at the Radiumhemmet, Stockholm, between 1914 and 1942. The methods of treatment and results have been described in previous reports by this author and his coworkers in the *British Journal of Radiology* and *Acta Radiologica* and are given in less detail in the present communication.

Charts, diagrams, and pictures are used to illustrate the author's methods and beliefs. The improvement in five-year results in cancer of the uterine corpus is attributed to the use of the "packing method" of radium application; whereas the improvement in five-year results in cancer of the cervix is accredited to better judgment accruing from experience.

R. S. MACINTYRE, M.D.
(University of Michigan)

Transurethral Resection and Deep X-Ray Therapy in the Surgical Management of Cancer of the Bladder. Luis F. Torres, Jr., and Paterno S. Chikiamco. J. Philippine M. A. **23:** 453–454, October 1947.

During the last six years, among 1,432 urological patients, 37 cases of papillary carcinoma of the urinary bladder were encountered on cystoscopic examination, and in each instance the diagnosis was confirmed histologically. Twenty-seven of the patients had transurethral resection of the vesical neoplasm. No patient was denied a resection except in the presence of metastases or a small urethra which could not accomodate the instrument. Six of the 27 patients required two to three resections in order to extirpate the tumor completely. From 3 to 49 gm. of tissue were removed in these cases. One to two weeks after the last resection, deep roentgen therapy was given, with the standard 200-kv. technic for a total of 3,000 to 12,000 r, depending on the degree of resistance of the tumor, the reaction of the skin, and the general condition of the patient. Check-up cystoscopies were done usually every two months for one year thereafter, and every six months for the rest of the five-year period of observation.

Three patients in the series have died: one male patient from uremia, a female from rupture of the bladder through the site of the tumor, and one male patient from coronary thrombosis associated with arteriosclerotic hypertension. One male patient had a recurrence. There are 6 patients in whom a five-year survival has been proved. These patients are alive and free from evidence of tumor either in the bladder or elsewhere as shown by cystoscopy and radiography. Seventeen patients are unaccounted for. The authors make no claims for this method of treating bladder cancer, but believe it has some advantages over open cystostomy.

Nitrogen Mustard as a Therapeutic Agent for Hodgkin's Disease, Lymphosarcoma and Leukemia. Maxwell M. Wintrobe, Charles M. Huguley, Jr., Margaret T. McLennan, and Lucio Penna de Carvalho Lima. Ann. Int. Med. **27:** 529–540, October 1947.

The biologic effects of nitrogen mustard have been shown to be parallel and almost identical with the biologic effects of radiant energy. As a therapeutic agent it offers the advantages of ease of administration and availability, under conditions where roentgen therapy may not be obtainable. The most significant objection to its use is that it is a potent hemopoietic toxin, with a narrow margin of safety between the therapeutic dose and the serious toxic dose. Frequent careful hematologic examinations are, therefore, mandatory in cases receiving nitrogen mustard therapy.

The authors have treated 77 cases of Hodgkin's disease, lymphosarcoma, leukemia, and certain miscellaneous disorders. In all of these cases the hydrochloride salt of di(β-chloroethyl)methyl amine ($CH_3N(C_2H_4Cl)_2$) was used. To 10 mg. of the dry white crystalline hydrochloride salt of the mustard, obtainable in small sterile bottles, 10 c.c. of sterile physiologic saline are added. The solution is immediately introduced into the vein through a rubber tube through which a saline infusion has already been started. It is important that the nitrogen mustard be injected promptly after it has been dissolved, as its activity is quickly dissipated.

The dosage has usually been 0.1 mg. per kilogram of body weight. As a rule, four to six infusions have been given at intervals of one or two days, depending on the presence or absence of severe toxic symptoms. In patients with chronic leukemia or Hodgkin's disease who have already responded to nitrogen mustard therapy, maintenance therapy has been carried out by giving two or three infusions on successive days at intervals of two to four weeks, without hospitalizing the patient.

Hodgkin's Disease: Of 28 patients with Hodgkin's disease, 15 are living at the present time and 13 are dead. In 6 patients (21 per cent) the results were definitely poor; in 17 (61 per cent) they may be classified as good, while in 5 (18 per cent) the response could be characterized as only fair.

Lymphosarcoma: In this group of 11 cases great individual variation was observed, from a remarkable melting away of the tumor following treatment, with long remission, to essentially no benefit whatever.

Leukemias: Of 8 cases of chronic myelocytic leukemia, one was terminal on admission and resistant to roentgen therapy. In 3 of the remaining 7 patients, good results were obtained. Where a favorable response to therapy has been achieved, there has not only been a reduction in the white cell count to normal, but the platelet count has returned to normal and anemia has been relieved. At the same time the spleen has been reduced in size, there has been a gain in weight, and a sense of well being has returned. Thus the effect has been similar to that which is observed following roentgen therapy.

Of 10 patients with chronic lymphocytic leukemia, 3 are in remission nine to twenty-six months after therapy was first given. Eight patients with acute or subacute forms of leukemia have been treated, with "poor" results in 5 and "fair" results in 3.

In general, the effect of nitrogen mustard on the blood was found to be biphasic: (1) an initial depression of leukocytes, and sometimes of platelets and red cells; (2) a later therapeutic effect usually corresponding with the degree of general improvement. Not only in cases of chronic leukemia, but also in patients with Hodgkin's disease, the leukocyte and platelet counts returned to normal and anemia disappeared.

No definite correlation was found in any of the cases between the fall in red cell level and the size of the dose administered. It appeared that in the dosage used, nitrogen mustard rarely produced anemia in cases of Hodgkin's disease and lymphosarcoma.

Some degree of nausea and vomiting occurred in nearly every patient given nitrogen mustard.

Unfortunately, the response to nitrogen mustard seems to be largely unpredictable and consequently a therapeutic trial must, in the last analysis, give the answer as to whether this agent is likely to be beneficial in a given case. A salutary effect upon lymph nodes, fever, splenomegaly and various clinical symptoms was observed in many patients with Hodgkin's disease, lymphosarcoma, and leukemia. Ultimately, however, nitrogen mustard, like irradiation, has proved ineffective in many cases. STEPHEN N. TAGER, M.D.

Vascular Nevi of the Skin: Considerations on Treatment. Alfredo Mario Segers. Prensa méd. argent. **34:** 2014–2016, Oct. 17, 1947.

While working as a Fellow in Surgery in the Tumor Clinic of Harvard University Medical School, the author made observations on a group of patients treated in infancy for vascular nevi of the skin. He discusses refrigeration, sclerosing injections, radon seeds, and surgical treatment.

These lesions have responded to irradiation, both with x-rays and with radium, in suberythematous doses. The results obtained by radium have been excellent. Some of the cases observed over twenty-five years, however, have shown atrophic telangiectatic skin over the affected zone, sometimes keratoses, and in one case epithelioma. Such changes have tended to direct the therapy of vascular nevi away from irradiation.

The residual scar, following treatment with carbon dioxide snow or sclerosing injections, may also be the site of neoplastic change but statistics indicate that the percentage of malignant degeneration in this type of scar tissue is much less than with an irradiation scar. However, the use of snow or of the sclerosing solution may have to be supplemented with radon seeds. The latter are indicated in deep vascular nevi which have not responded to other treatment, but they are contraindicated in lesions located near osseous epiphyses in children and in the eyelids. Surgical treatment is needed in certain lesions, especially in the eyelids, and in some others which do not respond to sclerosing injections. JAMES T. CASE, M.D.

The Use of X-Rays for the Treatment of Hypertrichosis Is Dangerous. Anthony C. Cipollaro and Marcus B. Einhorn. J. A. M. A. **135:** 349–353, Oct. 11, 1947.

This paper, published under the authorization of the Council on Physical Medicine of the American Medical Association, is a warning against the use of x-rays for the treatment of hypertrichosis, directed especially against organizations sponsoring the use of x-ray machines by inexperienced operators for cosmetic purposes. A considerable number of case histories illustrating the serious sequelae of such treatment are included.

"The immediate results of radiotherapy of hypertrichosis," say the authors, "are always good. It takes months or years for radiodermatitis to develop, and it takes even longer for the keratoses, ulcerations, malignant growths and death to occur. It is to be hoped that the manufacturers of x-ray apparatus in this country will not produce equipment to sell to those endangering the health of American people with x-ray burns and cancer. . . . The local health authorities, the chambers of commerce, the better business bureaus, the legislative committees and all civic organizations concerned with the guarding of the health of the public should join forces and nip in the bud the spread of organizations using x-rays for the permanent removal of unwanted hair."

Results of Repeated Epilation with Roentgen Rays in Tinea Tonsurans. H. H. Hazen. Arch. Dermat. & Syph. **56:** 539–540, October 1947.

In a brief note the author warns against the performance of more than two standard roentgen-ray epilations in tinea tonsurans (or capitis). In 5 Negro children in whom three treatments were given, regrowth of hair was satisfactory after the second epilation, but after the third the reappearance of hair was delayed for a matter of months; the regrowth was dry and scanty, and many of the hairs showed alternate rings of black and white.

Beta Irradiation in Ophthalmology. Charles E. Iliff. Arch. Ophth. **38:** 415–441, October 1947.

Beta radiation applied with the special applicator of Burnam, which contained 200 to 500 millicuries of radon, was found to give excellent results in vernal conjunctivitis. Sixty patients were treated, with cure in 30 per cent, improvement in 63 per cent, and no improvement in 7 per cent. Forty-one patients had palpebral lesions, 12 limbal lesions, and 7 a combination of palpebral and limbal lesions.

In tuberculosis of the anterior ocular segment, beta irradiation seemed to shorten the course and decrease the severity of the symptoms, with less residual scarring of the cornea. Of 72 eyes treated, the lesions of 52.8 per cent were considered healed after treatment; the condition of 38.9 per cent was improved, and that of 8.3 per cent showed no improvement in spite of adequate treatment. Vision was improved two lines or more in 42 per cent of the eyes, maintained in 46 per cent, and decreased in 12 per cent. Irradiation, however, did not prevent recurrences of tuberculosis.

Small benign tumors of the anterior ocular segment proved easily and safely removable by beta irradiation, with excellent cosmetic results. The procedure is particularly satisfactory for work with children.

Of 5 patients with typical punctate keratitis treated by beta irradiation, only one showed improvement. In the treatment of corneal scars in which vascularization was a prominent feature and there was still activity, irradiation appeared to be beneficial. With old, calcified and dense scars, treatment was not successful. Beta irradiation is ideal for preventing superficial vascularization after keratectomy and keratoplasty.

Eighteen patients with pterygiums were treated with beta irradiation; in only 1 did treatment seem slow in yielding results, and operation was performed. Conjunctival flaps over the cornea and granulation tissue were flattened and made avascular.

Corneal dystrophies, sarcoid, lupus erythematosus, pemphigus, punctate keratitis, and corneal ulcers due to pyogenic infections are not benefited by beta rays, and may be made worse by their use.

Beta Ray Radium Applicator for Ocular Use. Preliminary Report. Charles E. Iliff. Arch. Ophth. **38:** 827–830, December 1947.

A beta-ray radium applicator for ocular use is described. The time of application is greatly increased, and its use as compared with that of the Burnam radon applicator is limited. In the radon applicator, there is a point source of radiant energy ranging from 200 to 500 millicuries, with a very short half-transformation time. The new radium applicator, on the other hand, has a low potential, a wide surface fire, rather than a point fire, and what might be termed an unlimited life expectancy. Owing to the low potential and the surface fire, the use of the radium applicator is limited to treatment of vernal conjunctivitis, tuberculous sclerokeratitis and small tumors of the anterior segment, and to the prevention of overgrowth of fibrous tissue. It is not useful in the occlusion of vessels. The instrument should be applied by a holder of some form. The precautions applicable to all radiation therapy should be observed.

It is felt that the radium applicator, although it cannot duplicate the performance of the radon applicator, will fill a definite need in the treatment of the lesions mentioned.

On Roentgen Treatment of Scleritis. Olaf Blegvad. Acta ophth. **25:** 397–404, 1947.

Forty-three cases of scleritis (among some 102,600 cases of ophthalmic affections treated over a twenty-year period) have received roentgen therapy at the Finsen Institute and Radium Center, Copenhagen. It was possible to follow-up all but 2 of this group. The Wassermann reaction was negative in all. Of the 41 followed cases, 36 were in women. The distribution according to the type of the disease was: episcleritis and scleritis, 24 cases; keratoscleritis, 8 cases; kerato-iridoscleritis, 9 cases. The treatment factors were: 50 r, three times, at weekly intervals; filtration in most instances 0.5 mm. copper; focus distance 40 cm. Immediately after the treatment there was usually a slight reaction, consisting of pain and injection, but on the following day pain had generally disappeared. Swelling and injection usually did not disappear until some time after the third and final treatment. When the first series of treatments did not produce relief from symptoms, it was repeated after a suitable lapse of time. Thirty-one patients had one series of treatments, 3 had two, 5 had three, 1 had four, and 1 had eight.

In 35 cases the results were considered "good," *i.e.*, the pathologic process quieted down completely and there were no recurrences. In the remaining 6 cases the results were poor. As might be expected, roentgen therapy is of the greatest value in uncomplicated scleritis, but it also seems of value in sclerokeratitis and sclerokerato-iritis.

Osteitis Pubis Following Suprapubic Prostatectomy. Results with Deep Roentgen Therapy. Albert E. Goldstein and Seymour W. Rubin. Am. J. Surg. **74:** 480–487, October 1947.

Four cases of osteitis pubis following suprapubic prostatectomy are added to the literature and attention is

drawn to the success which has accompanied the use of deep roentgen therapy.

A review of the literature on osteitis pubis shows that this condition follows (1) some trauma to the symphysis and pubic bones and (2) infection of the traumatized areas. The trauma causes a devitalization of the tissues and a superimposed infection comes from a very accessible source—the prevesical area—potentially infected by the urine following suprapubic prostatectomy. The condition almost always follows suprapubic prostatectomy but has been reported (1) following infected herniorrhaphy, (2) after post-traumatic prevesical abscess persisting after incision as a suprapubic sinus, and (3) following trauma to the lower abdomen.

All cases present a similar pattern. The main signs and symptoms usually develop two weeks following surgery but can occur as late as two months. Groin pain with abductor spasm in one or both thighs is present in all. This abduction pain may be partially relieved by adduction. Pain radiates down one or both extremities and may prove incapacitating.

Diagnosis is established roentgenographically. The first examination may show nothing, but soon there is a separation of the symphysis pubis with a fluffiness of the periosteum. Later osteoporosis is evident.

Factors in the roentgen therapy of three of the cases are given, as follows:

Case I: 200 kv.; 20 ma.; 50 cm. target-skin distance; 15 × 15 cm. portal. Anterior left hip: 2,020 r (over period of 1 month); lateral left hip: 1,820 r (over period of 1 month); posterior left hip: 1,030 r (over period of 1 month).

Case II: 200 kv.; 20 ma.; 50 cm. target-skin distance; composite filter. Anterior symphysis: 2,435 r to a 10 × 10 cm. portal (over period of 5 months); posterior symphysis: 2,200 r to a 15 × 15 cm. portal (over period of four months).

Case III: 200 kv.; 20 ma.; 50 cm. target-skin distance; 2 mm. Cu filter; 10 × 10 cm. portal. Anterior symphysis: 6,668 r (over period of 1 year).

JOSEPH P. TOMSULA, M.D.

RADIOACTIVE ISOTOPES

Urinary Excretion of Radioactive Iodine, I^{131}, in a Case of Severe Hyperthyroidism. K. W. Stenstrom and J. F. Marvin. Proc. Soc. Exper. Biol. & Med. **66:** 47–49, October 1947.

Radioactive iodine, 9.1 millicuries of I^{131}, was administered orally to a female patient, aged 29, suffering from a severe hyperthyroidism of diffuse type with marked exophthalmos. Lugol's solution had been given for a period of several months but had produced only brief improvement and was discontinued three weeks before the radioactive iodine was started. Urinary excretion was determined by means of a beta-ray Geiger-Müller counter. The total retention of radioactive iodine after two days was 54 per cent. Three millicuries of I^{131} was given about six weeks later. The urinary excretion was again determined, and the retention after one day was found to be 85.5 per cent. Stable iodine in the form of Lugol's solution was administered for a period of two days after the urinary excretion of I^{131} had reached a low level. This was followed, each time, by excretion of I^{131} in relatively large amounts, beginning some twenty-four hours after the stable iodine was given and lasting for some forty-eight hours after it was discontinued. At the time of the report the patient's condition had improved somewhat and she had gained weight, but no decided reduction of the basal metabolic rate occurred in the first two months following the first dose of I^{131} and it seemed probable that further treatment would be required. An increase in excretion of I^{131} was not observed following administration of Lugol's solution in one case of carcinoma of the thyroid with metastasis.

Influence of Radioactive Phosphorus on Tumour Growth in Mouse Tumour C.2146 and Brown-Pearce Rabbit Carcinoma. A. Forssberg and F. Jacobsson. Acta radiol. **28:** 391–399, Aug. 30, 1947.

Radioactive phosphorus (P^{32}) was administered intraperitoneally to mice grafted with the tumor C.2146 and the growth of the tumor was followed. Even dosage as high as 60 microcuries had little influence when given on six consecutive days with the first injection at the time of grafting. When the first dose was given twenty-four hours before the graft, however, disappearance of the tumor was frequently observed. The quantitative relation between tumor growth and dosage was also studied after a "prophylactic" treatment with P^{32}, in the hope of finding a suitable dosage which would check tumor growth without being lethal. In certain concentrations, P^{32} was found to inhibit tumor growth. Deaths occurred among the animals, however, and it seems to be difficult to find a concentration range in which P^{32} is effective as a therapeutic agent but produces no deleterious effects on the body. Only a few experiments were carried out with the Brown-Pearce carcinoma, and from these no conclusions are drawn.

EFFECTS OF RADIATION

Morphologic Changes in the Lymphocytes of Persons Exposed to Ionizing Radiation. Annamae Dickie and Louis H. Hempelmann. J. Lab. & Clin. Med. **32:** 1045–1059, September 1947.

This is an excellent presentation from the Los Alamos Scientific Laboratory (University of California). By the use of supravital stains it was found that the lymphocytes of persons exposed to radiation and toxic chemicals contained more refractive neutral red bodies than did the cells in the blood of persons not thus exposed. These bodies, previously described in normal lymphocytes by Gall (Am. J. M. Sc. **191:** 380, 1936), were irregularly placed through the cytoplasm and with the stain used had a decided brick-red color. The number of bodies per cell varied from one to more than thirty. A cell containing more than five was considered to be abnormal. The number of lymphocytes containing an abnormal number of these bodies was found to be increased, even in persons who had not exceeded the customary tolerance dose of 0.1 r per day.

The staining technic is fully explained, and excellent photomicrographs of the blood smears are reproduced. Interesting charts are presented for statistical study.

The authors' conclusions are as follows:

1. Analysis of the total leukocyte counts of persons chronically exposed to ionizing radiation and toxic chemicals shows a significant statistical decrease in the exposed groups.

2. Analysis of the absolute number and of the percentage of lymphocytes in the differential counts of the same persons shows no significant change.

3. Morphologic study of supravital preparations of blood cells of persons chronically and acutely exposed to ionizing radiation indicates a striking increase in the number of refractive neutral red bodies in the cytoplasm of the circulating lymphocytes. An increase in neutral red bodies is also found in persons working with toxic chemicals.

4. These neutral red bodies have high density and may be considered to be granules. They have not been identified in fixed preparations.

This would appear to be a very important article, as it seems to open up an entirely new approach to the problems regarding the biological effects of total body irradiation. EVERETT L. PIRKEY, M.D.

Gastric Ulcer Following Radiation. Frank E. Hamilton. Arch. Surg. **55:** 394–399, October 1947.

Of 256 patients with tumors of the testis treated with million-volt x-rays at Walter Reed General Hospital, about half experienced epigastric distress from two to three months after irradiation. In 35 a large single gastric ulcer was found on fluoroscopy. All of this group had received doses in excess of 5,000 r to the region of the stomach. The outstanding symptom was epigastric distress; some experienced pain relieved by food, some pain unrelated to food, and some gastric hemorrhage. Gastric acidity was sometimes decreased, but was often normal. Most of the patients responded to medical management, but in 6 operation was necessary. Of these, 4 were clinically cured, 1 was improved, and 1 died postoperatively.

The brown leathery skin healed well after operation. Within the abdomen, there was fibrosis of the irradiated tissues, and usually increased vascularity. The stomach and jejunum had a brown, burned-out appearance. The dome of the diaphragm was high, and the stomach pulled up. The mesentery of the colon and jejunum was shortened, and the omentum was a small, burned-out shred. The affected portions of the stomach and jejunum were smoothed out and no peristalsis was visible.

In all 6 operated cases the ulcer was on the posterior wall of the stomach near the pylorus. Two ulcers had perforated into the pancreas with encapsulation of the abscess. A case is also mentioned in which a patient known to have a radiation gastric ulcer died of generalized peritonitis and at autopsy was found to have two perforated ulcers of the ileum.

LEWIS G. JACOBS, M.D.

Comedos Following Roentgen Ray Therapy. Samuel M. Bluefarb. Arch. Dermat. & Syph. **56:** 537–539, October 1947.

The appearance of comedos in a zone surrounding the scar following roentgen therapy for an epithelioma of the face was observed by the author. The patient was beyond the age at which acne occurs, and there was no evidence of comedos prior to irradiation. It is assumed that the comedos were due to an irritation of the follicles of the sebaceous glands immediately surrounding the roentgen-ray scar, and it is believed that they represent a compensatory hypertrophy of the sebaceous apparatus.

Some Observations on Radiation Sickness and Its Treatment. Stig Kullander. Acta radiol. **28:** 221–224, June 30, 1947.

The author has found dilute hydrochloric acid (20 drops in water four times daily before meals) quite effective in controlling radiation sickness. Evidence of achlorhydria was obtained in 50 of 54 vomits (*sic*) of patients with radiation sickness and of hypochlorhydria in the remaining 4. In 10 of these same patients gastric acid was normal after irradiation had been discontinued, an indication that in radiation sickness there is an insufficient production of hydrochloric acid even in patients in whom acidity is normal under other conditions.

The author is not in agreement with the theory that histamine causes radiation sickness. He has, in fact, given histamine to 4 patients with radiation sickness just before eating. In all these patients the radiation sickness was alleviated and vomiting ceased.

[*Abstractor's Note:* Since reading this article I have used dilute hydrochloric acid in the management of 6 patients with radiation sickness. All were helped considerably and 4 were completely cured after two to three days.] JAMES C. KATTERJOHN, M.D.

Effect of Roentgen Irradiation on Epiphyseal Growth. Experimental Studies upon the Dog. John A. Reidy, James R. Lingley, Edward A. Gall, and Joseph S. Barr. J. Bone & Joint Surg. **29:** 853–873, October 1947.

An experiment was performed to determine the effect of irradiation upon epiphyseal growth. Twelve puppies of both sexes were divided into three groups of four animals. The first group received 800 r, the second 1,000 r, and the third 1,200 r to the right knee and the left wrist. Seven weeks after treatment, small metallic markers were inserted into the diaphysis of each irradiated tibia and radius at approximately the mid-shaft. This was done to determine the amount of growth contributed by this epiphysis. One dog of each group was sacrificed at varying intervals to determine the histologic change in the bone and joint. The effect of the irradiation on the length of the treated extremity progressed for about six months, after which there was no appreciable change.

The effect of the irradiation was seen in the shortening and bowing of the treated limb and discoloration and thinning of the hair over the site of irradiation. From frequent radiographic measurements of the extremities, graphs were made to show the amount of change that occurred.

Degenerative changes were found in the articular cartilages of the irradiated joints. It could not be definitely decided, however, whether the changes were due to the irradiation or to the deformity produced in the bone as a result of the irradiation. Additional study on this phase must be made.

JOHN B. MCANENY, M.D.

Effects of Roentgen Irradiation on the Testes of Rabbits. Possible Harmful Effects on Human Testes from Low Voltage Roentgen Ray Therapy. J. Lamar Callaway, Vince Moseley, and Sherwood W. Barefoot. Arch. Dermat. & Syph. **56:** 471–479, October 1947.

In order to determine whether or not low-voltage roentgen therapy is attended by potential danger of accidental injury to the gonadal tissues of men, an attempt was made to measure the scattered radiation to

which the gonads might be exposed during the course of irradiation of the face, and studies were also made as to the effect of direct irradiation on the testes of rabbits and of man.

The methods used to study the intensity of irradiation at the level of the testes during treatment of the head and neck appear to be rather crude and if made as shown in an accompanying illustration would be totally inconclusive, because of the physical set-up.

The article, however, does give a good review of the effects of radiation on animal and human testes. It is pointed out, by way of introduction, that while data concerning the tolerance of the testis for roentgen rays are notably lacking, it has been shown that the resistance of fully developed spermatogonia is considerably greater than the resistance of the spermatocytes or spermatids as found in the semen. It has been shown further that fertile spermatozoa may persist in animals for as long as six to twelve weeks after administration of known sterilizing doses of roentgen rays.

The authors attempted to suppress spermatogenesis in rabbits with gradually increasing doses of unfiltered low-voltage roentgen rays from 950 to 1,500 r. The number of animals used is small, but as the successive doses reached between 650 and 950 r, the sperm count would drop to zero. For producing permanent sterility, doses above 950 r were required.

Observations were also made on two patients with carcinoma of the prostate who were given x-ray irradiation previous to orchiectomy. No apparent arrest of spermatogenesis was produced by 300, 600, or 900 r.

SYDNEY F. THOMAS, M.D.

Effects of X-ray Irradiation on Viscosity of Synovial Fluid. Charles Ragan, Charlotte P. Donlan, James A. Coss, Jr., and Audrey F. Grubin. Proc. Soc. Exper. Biol. & Med. **66:** 170–172, October 1947.

The viscosity of normal human synovial fluid is very high. Joint fluid obtained from the knees of patients with rheumatoid arthritis tends to be of greater viscosity in the chronic stage of the disease than in the acute stage, and to approach the viscosity of normal synovial fluid.

Studies carried out by the authors showed that (1) the viscosity of joint fluid is decreased by exposure to x-rays, the decrease in viscosity being directly proportional to the amount of irradiation. (2) The viscosity of pure hyaluronic acid solutions is decreased less by the action of x-rays than is the viscosity of joint fluid. (3) Joint fluid is as susceptible to the enzymatic action of bull testis hyaluronidase in the irradiated sample as in the control. No increase in titratable acidity follows irradiation of pure hyaluronate solution, indicating that the reduction in viscosity probably does not result from oxidative degradation. (4) The possible physiological implications are discussed.

Quantitative Histological Analysis of Radiation Effects in Human Carcinomata. Brigitte Wolff and Frank Ellis. Brit. J. Radiol. **20:** 381–386, September 1947.

An evaluation of the effects of radiation on 37 cases of carcinoma from various sites by the differential count method of Glücksmann (Brit. J. Radiol. **14:** 187, 1941. Abst. in Radiology **38:** 125, 1942) was made. Biopsies were done immediately before treatment and after seven, fourteen and, in most cases, twenty-one days. By counting the numbers of resting, mitotic, differentiating, and degenerating cells in each series of biopsies,an indication of the ultimate result is obtained. The outlook is favorable if the resting and mitotic cell counts fall and the degenerating and differentiating cells rise. The outlook is unfavorable if there is little change in the counts, or if nests of malignant cells are observed in the later biopsies.

Agreement was obtained between histological findings and clinical findings in 31 out of the 37 cases. In the 6 cases in which disagreement was found, the histologic indication was unfavorable.

This method offers a possibility of detecting at an early stage of treatment, possibly within four weeks, those cases which are going to show an unfavorable response to irradiation, so that if other methods of treatment are available, they may be applied before months of time are lost. SYDNEY J. HAWLEY, M.D.

Experiments on the Mechanism of the Biological Action of Fast Neutrons, Using the Summation Method for Lethal Effects in Mice (With a Section on Dosimetry of Fast Neutrons). J. S. Mitchell. Brit. J. Radiol. **20:** 368–380, September 1947.

Experiments were undertaken (1) to determine whether or not the relevant mechanisms of the biological action of fast neutrons are identical with those of gamma radiation and particularly whether the two radiations are completely additive; (2) to measure the relative efficiency per unit of energy absorption and to determine whether this increases with over-all time of exposure.

Mice were exposed to whole body irradiation of both types for two different time periods, twenty-four and forty-eight hours, and to mixtures of the two radiations in various proportions and in various order. The criterion used as an end point was death within twenty-one days after the irradiation.

Dosage was measured by means of small ionization chambers. The dose from fast neutrons was determined by measurement of the absorption of the ionization in lead, and is expressed in roentgens. One roentgen from neutron irradiation is that amount which produces the same energy absorption per unit volume of tissue as is produced by 1 r of the usual filtered gamma radiation. The neutrons came from a polonium-beryllium source.

In the twenty-four-hour series the neutron dose was 35.4 r and the gamma ray dose 1,000 r. In the forty-eight-hour series the neutron dose was 47.2 r and the gamma ray dose 2,000 r.

A significant departure from additivity was found in both series. The mixed dosages were less lethal than either type of irradiation alone. The relative biological efficiency of fast neutrons, in terms of the efficiency of gamma radiation as unity, was found in the experiments with a mean exposure time of forty-eight hours to have the approximate value of 32.0 ± 8.6. This value is significantly greater than for short exposures.

These findings indicate that there is a difference in the mechanism of action of the two types of radiation. A plausible explanation is that the cells most sensitive to gamma radiation are those in mitosis, particularly prophase, and that, in part at least, the gamma ray effect is due to chromosome interchange. The cells are more uniformly sensitive to neutrons throughout their life cycle. SYDNEY J. HAWLEY, M.D.